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THE EFFECT OF CERTAIN HORMONES ON TISSUE RESPIRATION AND PHOSPHORUS METABOLISM

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by

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ABSTRACT

The effects of hypophysectomy and adrenalectomy, and the administration of certain hormones on the QO_2, acid soluble phosphorus concentration and P^{32} incorporation, were studied in selected tissues of the male rat and guinea pig. The tissues studied were plasma, adrenal gland and the dorsolateral prostate and ventral prostate glands. The hormones employed were adrenocorticotropic hormone (ACTH)and desoxycorticosterone acetate (DCA).

Hypophysectomy was found to cause a decrease in the concentration of the inorganic phosphorus of the plasma, but a much greater increase in the specific activity. ACTH, administered intraperitoneally as a single injection, increased the plasma phosphorus concentration in hypophysectomized rats toward normal but had little effect in intact animals. Injection of ACTH did not affect the plasma specific activity in either normal or hypophysectomized animals.

Hypophysectomy reduced the QO_2 and relative specific activity of the adrenal. In hypophysectomized animals, the adrenal acid soluble phosphorus concentration was increased. Administration of ACTH increased the adrenal QO_2 and relative specific activity in both hypophysectomized and intact animals.

In hypophysectomized rats, the dorsolateral prostate and ventral prostate QO_2 were reduced. In contrast, the phosphorus

concentration and specific activity were increased in these animals. Twenty-four hours after a single injection of ACTH, intact guinea pig prostate QO_2 was increased, however, this treatment had little effect on dorsolateral prostate or ventral prostate QO_2 in either intact or hypophysectomized rats. No changes were observed in prostate phosphorus concentration or specific activity after ACTH had been administered to hypophysectomized rats. In intact animals, administration of ACTH slightly increased the phosphorus concentration and specific activity in guinea pig prostate, but, in contrast, ACTH, in one set of experiments, reduced rat ventral prostate specific activity.

The plasma phosphorus concentration was increased after adrenalectomy or chronic DCA treatment of intact rats. An increased plasma specific activity was found in adrenalectomized animals. Daily injections of DCA slightly decreased plasma specific activity in both adrenalectomized and intact rats.

A single injection of DCA increased adrenal QO_2. However, chronic DCA treatment slightly decreased both the adrenal QO_2 and the adrenal relative specific activity.

Adrenalectomy and daily injections of DCA in intact rats reduced dorsolateral prostate QO_2. After adrenalectomy, the dorsolateral prostate relative specific activity was also reduced.

The ventral prostate QO_2 and relative specific activity were not affected by adrenalectomy or by chronic DCA treatment.

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I. INTRODUCTION

The adrenal glands were apparently first described by Eustachius in the sixteenth century (1). The importance of the adrenal glands was appreciated only after Addison (2) associated the disease which now bears his name with destructive lesions in the glands. His observations interested the physiologist Brown-Séquard, who made the pioneer experiments on the effects of adrenalectomy and concluded that the adrenal glands were essential to life (1). The classical study of Smith (3) established the fact that hypophysectomy results in atrophy of the adrenal cortex.

Numerous studies have served to elucidate the physiology and biochemistry of the adrenal cortex and medulla but few investigations have been conducted on the metabolic pattern underlying the endocrine phenomena of these tissues. The respiratory rate coupled with an examination of the incorporation of radioactive phosphorus offers a convenient method for the examination of the metabolic activity of a tissue.

This investigation was primarily designed to study the effects of various experimental conditions on the tissue respiration and phosphorus metabolism of the adrenal gland. In addition, the effects of altered adrenal states upon the tissue respiration and phosphorus metabolism of the dorsolateral

prostate and ventral prostate were studied. Previous workers in this laboratory have studied the effect of altered adrenal states upon the zinc metabolism in the rat adrenal and prostate. Rudzik and Riedel (4) and James (5) postulated a dependence of the dorsolateral prostate on normal adrenal activity since they had observed that adrenalectomy decreased the zinc concentration and Zn^{65} incorporation in this gland.

A series of experiments was conducted on the effect of hypophysectomy and the administration of adrenocorticotropic hormone (ACTH) on the tissue respiration and P^{32} uptake in the adrenal gland and prostate glands. A second series of experiments was conducted on the effect of desoxycorticosterone acetate (DCA) on the respiratory rate and P^{32} incorporation in the same tissues. The effect of adrenalectomy and the administration of DCA on the prostate glands was also studied in the second series.

II LITERATURE SURVEY

A. THE ADRENAL CORTEX

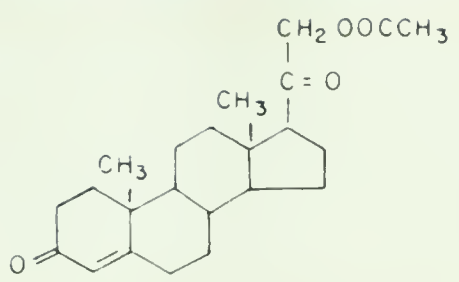
1. Adrenocortical steroids

Adrenocortical hormones were first isolated from the adrenal gland in 1936 (6). By 1958, over 40 steroids had been isolated from adrenal extracts (7). Of the biologically active steroids secreted in the adrenal venous blood, cortisol and corticosterone are quantitatively the most important (8). Smaller amounts of some C_{19} and C_{21} steroids were found in the adrenal effluent after corticotropin stimulation (8). Aldosterone, while of great physiological importance, is secreted by adult human subjects in very small amounts, of the order of 200 micrograms per day (9). It has been estimated that an adult human subject secretes about 25 milligrams of cortisol per day (10).

The sequences of reactions involved in the biosynthesis of adrenocortical steroids are not fully known. Both acetate and cholesterol labelled with C^{14} have been incorporated into corticosteroids (11). Although cholesterol would seem to be an obvious potential precursor of the adrenocortical hormones (12), whether it is an essential intermediate in the synthesis of corticosteroid hormones from acetate is a controversial question (13). An enzyme system has been found in adrenal glands which is capable of cleaving cholesterol to pregnenolone and isocaproic

acid (14). Another enzyme system (12) converts the Δ^5-3 beta hydroxy compound, pregnenolone, into the Δ^4 - 3 - oxosteroid, progesterone. It is postulated that the various adrenocortical hormones are biosynthesized by a series of enzymatic hydroxylations and dehydrations at the 11 beta, 17 alpha, 18, and 21 positions of progesterone (12, 13, 15).

11-Desoxycorticosterone has been isolated from beef adrenals, but it is normally secreted in very small amounts (12). The formula of desoxycorticosterone acetate (DCA) is shown.



2. Relation of steroid secretion to the histological zones of the adrenal cortex.

The adrenal gland was histologically divided into concentric zones, the outer connective tissue capsule, the zona glomerulosa, zona fasiculata, zona reticularis, and central medulla by Arnold in 1866 (16). Gottschau (17) suggested that adrenal cells formed under the capsule and migrated to the zona fasiculata where they elaborated their secretions, and died in the zona reticularis. The theory of cell migration was replaced by the zonal theory (12). This theory suggested that there may be a division of secretory function between the zones of the adrenal

cortex and that these functions may not be equally dependent upon the hypophysis. This theory was based on the observation that electrolyte imbalance followed adrenalectomy but not hypophysectomy. Also, after hypophysectomy, the zona fasiculata atrophies, but the zona glomerulosa remains unchanged for some time. The work of Deane and Greep (18) supported the concept that an electrolyte active steroid was secreted by the zona glomerulosa, independent of the hypophysis, but subject to change according to electrolyte intake. By incubation of ox-adrenal slices, direct evidence was obtained which showed that aldosterone was preferentially produced by the zona glomerulosa and cortisol by the zona fasiculata (19). Further support for the zonal theory is the observation that the 17 alpha hydroxylating system is in the fasiculata only and that the 18 - oxidase is confined to the zona glomerulosa (20).

3. Transport and Metabolism of steroids

Binding of steroids to plasma proteins was first suggested by the fact that albumin greatly increased the solubility of steroids in aqueous media (21). By equilibrium electrophoresis of plasma to which hydrocortisone - 4 - C^{14} had been added, Daughaday (22) found a peak of radioactivity in the alpha globulin region. The corticosteroid-binding globulin (CBG) can bind a variety of steroids, and the relative affinity of the CBG for the steroid can be assessed by the ease with which it displaces C^{14} cortisol (22). According to Daughaday and associates (23), who compared the binding characteristics of sera from pregnant or estrogen-treated subjects to those of controls, increased binding of hydrocortisone - C^{14} can

be demonstrated by "estrogen" plasma.

Adrenocortical hormones are largely inactivated in the liver by reduction of the 20 - oxo substituent and/or the Δ^4 - 3 - oxo group in ring A. These reduction products are largely excreted as glucuronides (24). Blood (25) and muscles (26) have also been shown to be sites of corticosteroid inactivation. Studies on the metabolic transformation of hydrocortisone - 4 - C^{14} in normal men (27) revealed that eleven known metabolites accounted for approximately 90 per cent of the radioactivity in the urinary steroid fraction obtained after hydrolysis of conjugates with beta - glucuronidase. The major transformation products as a group were the tetrahydro derivatives. The glycerol side-chain derivatives, cortols and cortolones, accounted for 18 to 33 per cent. Cleavage of the side chain of hydrocortisone occurred to a limited extent.

4. Mechanisms of adrenocortical control.

Stimuli which activate adrenal corticoidogenesis include chemical agents, environmental conditions, and psychological phenomena (28). These stimuli were termed "stress" by Selye (29). The removal of the pituitary gland, which is the site of formation, storage and release of ACTH, prevents the activation of the adrenal cortex by stressful stimuli (28). The effects of ACTH on the adrenal cortex include stimulation or corticoid formation and content, increase in adrenal weight, and a decrease of ascorbic acid, lipid and cholesterol content.

Bovine ACTH is a 39 amino acid peptide (30). A synthetic peptide, the structure of which corresponds to the

postulated arrangement of the 23 amino acid residue from the amino end of the ACTH, is endowed with the full *in vivo* ascorbic acid depleting and plasma corticosterone elevating activity of the natural hormone (31). From a correlation of biological activity to the extent of oxidation of the methionine contained in the hormone, it is now concluded that the oxidation-reduction center of ACTH is the thioether grouping of methionine (32).

At least two mechanisms are involved in the control of ACTH release, one concerned with rapid responses to external environmental changes, the other with reciprocal adjustments to changing blood levels of adrenal cortical hormones. Both are probably mediated by the hypothalamus (28). Neural control over the release of ACTH is thought to be exerted by the secretion of a chemical mediator by the cells of the hypothalmic area of the brain into hypophysial portal vessels leading to the pituitary gland. The ACTH-releasing activity of vasopressin and its analogues, and an amino - acid analysis of an impure corticotropin-releasing factor (CRF) suggest that CRF is probably chemically related to vasopressin (33).

Stone and Hechter (34) found that ACTH stimulates the conversion of radioactive acetate and cholesterol to glucocorticoids but has no effect on the steroid - steroid conversions. They concluded that ACTH accelerates a rate-limiting reaction between cholesterol and pregnenolone. In a later paper, Hechter (35) concluded that hormones, including ACTH, probably act by influencing the passage of intermediates through the membranes of the cell. A recent hypothesis (36) postulates that the primary action of ACTH

is on the accumulation of adenosine - 3', 5' - monophosphate (3', 5' - AMP) within the adrenal cortex.

5. Physiological importance of adrenocortical hormones.

Cortisol excess produces fasting hyperglycaemia, glycosuria and an increase in liver glycogen. These effects are called adrenal steroid diabetes (12). This condition differs from pancreatic diabetes in that insulin does not lower the blood sugar level (37). Long and Luken (38) first showed an increase in urinary nitrogen when cortisone reversed the fasting hypoglycaemia of the adrenalectomized animal. They suggested the mechanism involved gluconeogenesis from protein catabolism. However, a similar study (39) showed that the production of glucose was in excess of that derived by gluconeogenesis. It was postulated that, in addition to their capacity to stimulate gluconeogenesis, the adrenocortical hormones also inhibit the utilization of carbohydrate by the tissues. In support of this thesis, it was shown that hexokinase activity was inhibited by adrenocortical hormones (40). Bacila and Barron (40) suggested that the hormones combine with the thiol groups of hexokinase to produce this inactivation.

The catabolic effect of cortisol, negative nitrogen balance, is accompanied by retardation or cessation of growth, muscle wasting, thinning of the skin, osteoporosis, and reduction in lymphoid tissue. Possible mechanisms of the anti-anabolic action have been suggested from experimental studies. High doses of cortisone decrease the incorporation of C^{14} glucose and amino acids into proteins of the diaphragm of both intact and adrenalectomized rats (41),

indicating prevention of protein anabolism. When the liver is surgically removed, amino acids, released from tissue proteins, cannot be deaminated and accumulate in the plasma. Plasma amino acids thus indicate the net rate of protein degradation. Exogenous steroids given to hepatectomized rats produced an accelerated rise of plasma amino nitrogen (42) indicating an increase in protein catabolism. Glucocorticoids facilitate the liver's ability to concentrate amino acids (43). This corticosteroid-induced "trapping" of amino acids by the liver may serve as stimulus for peripheral protein catabolism and degradation of amino acids by the liver.

The redistribution of body fat, increased centripetal fat at the expense of fat in the extremities, in patients receiving high doses of glucocorticoids or in patients with Cushing's syndrome, suggests both lipolysis and lipogenesis (44). The mechanisms involved are not precisely defined from experimental data.

Abnormalities in electrolyte and water metabolism associated with adrenal insufficiency, first described by Loeb and his co-workers (45), include excessive renal and extrarenal loss of sodium, potassium retention, decreased serum and intracellular sodium and increased serum and intracellular potassium. Since the plasma sodium levels of adrenalectomized rats were lower than the levels in neurohypophysectomized or in adrenalectomized-neurohypophysectomized rats and since antidiuretic hormone (ADH) depressed the plasma sodium concentration of the double operated rats (12), it was concluded that the naturetic effect of ADH potentiates the loss of sodium in adrenalectomized rats. The deficient diuretic response to water, characteristic of adrenal insufficiency (46) can be corrected

by a glucocorticoid (47).

Reduction in striated muscle function occurs in the absence of corticosteroids but small doses of adrenal extracts will reverse this effect (48). Similarly, the left ventricular work index of a rat heart-lung preparation has been shown to be exquisitely sensitive to minute amounts of corticosterone, cortisol and aldosterone, with aldosterone as the most potent (49). There is a close parallelism between the relative potencies of adrenocortical extracts and steroids in their ability to relieve the fatigue of muscle from adrenalectomized animals and their capacity to produce glycogen deposition in the liver (50).

A method employed clinically to evaluate the adrenocortical competence of a patient depends on the fact that the eosinophil cell count normally declines markedly after a dose of ACTH, while in a patient suffering from Addison's disease, such a decline is slight or absent (51). The eosinophil cell count in mice has been used successfully as a biological test for the potency of various adrenocortical steroids (52).

Adrenocortical hormones suppress the inflammatory reaction to tissue damage (53). The first important clinical paper on the effect of an adrenocorticoid was published in 1949 (54) describing the effect of cortisone in rheumatoid arthritis. The disease is alleviated primarily through the anti-inflammatory action of corticosteroid treatment (12).

Kerppola (55) reported an inhibitory effect of cortisone on oxidative phosphorylation and oxygen uptake by rat liver mitochondria which, through consequent reduction of ATP production, could presumably result in impairment of hexokinase

function, of oxidation of fatty acids in the Kreb's cycle, and of protein synthesis, and thus account for many of the symptoms of hypersecretion or excessive dosage of corticosteroids. Further studies by Kerppola and Pitkanen (56) indicated that the inhibitory effect of cortisone is located at the cytochrome oxidase level, since only minor or no changes were found in the succinic dehydrogenase and DPN-cytochrome - c reductase activities.

B. PHOSPHORUS METABOLISM

1. Plasma

Most of the phosphorus found in the plasma is present as the inorganic phosphate (57). In 1938, Anderson and Oestler (58) reported a marked fall in the concentration of plasma inorganic phosphate following removal of the pituitary in the rat. The decreased concentration of plasma inorganic phosphate in hypophysectomized rats has been confirmed by several workers (59 - 61). Li et al (61) observed that growth hormone prevents this decrease after hypophysectomy and even elevates the phosphorus level above that of the controls. ACTH has been reported to decrease the concentration of plasma inorganic phosphate in both normal and hypophysectomized rats (59). In contrast to this report, Riedel and co-workers (60) found that ACTH did not change the plasma phosphorus level in either normal or hypophysectomized rats.

When P^{32} is introduced into the plasma, most of the labelled phosphate ions soon leave it (62). The loss of labelled phosphate is partly due to its rapid diffusion into the extracellular space, to exchange with phosphorus atoms present in the cells of various tissues, and to excretion.

Gemzell and Samuels (59) found that the specific activity of plasma inorganic phosphate was higher in 5 day hypophysectomized rats than in normal rats, twenty minutes to twenty four hours after intraperitoneal injection of P^{32}. They suggested that a major factor in the difference of specific activities was a reduced extracellular space in the operated animals, and, in addition, a reduced rate of exchange of the inorganic P^{32} between the extracellular and intracellular compartments. Other investigators have also observed an increased specific activity of plasma inorganic phosphate in hypophysectomized rats (60, 63, 64). Geschwind et al (63) reported that the administration of growth hormone lowered this level toward normal. ACTH has been found to have no effect on the specific activity of plasma inorganic phosphate in either normal or hypophysectomized rats (59, 60, 65, 66).

2. Adrenal

In a quantitative histochemical study of the distribution of phosphorus compounds in the rat adrenal (67) it was found that cold trichloroacetic acid (TCA) extractable phosphorus is uniformly distributed in all zones and that there is a distinct peak in extractable ester phosphorus in the zona fasiculata. Injection of ACTH increases the inorganic phosphate (cold TCA) in all regions and increases the labile ester phosphorus in the zona reticularis and medulla. Fiala and Glinsmann (68) found there was a great loss in AMP in normal rat adrenal one hour after ACTH injection. On the other hand, ATP, which was quite low in the resting tissue, was very much increased as the result of hormonal stimulation.

Logan and co-workers (66) and Reiss and Halkerston (69) reported a significant increase in the specific activity of adrenal inorganic phosphate when ACTH was injected into normal rats. A trend in this direction was noted by other workers (59, 60, 65, 70) but the figures did not attain the conventional level of statistical significance.

It has been found that hypophysectomy decreases the incorporation of inorganic P^{32} into the total acid soluble phosphorus (69, 71) and inorganic phosphate (59, 60, 65, 66, 70-72) of the adrenal gland. In each instance, the changes brought about by removal of the pituitary were rapidly reversed by a single injection of ACTH. Evidence was presented by Logan, Riedel and Rossiter (73) for the suggestion (59) that the decreased specific activity of inorganic phosphate in adrenals of hypophysectomized rats is due to a decrease in the rate at which P^{32} passes through the membrane of the adrenal cell.

Riedel et al (65), finding both the concentration and the uptake of P^{32} into lipid-phosphorus decreased in adrenals of hypophysectomized rats, suggested that in the hypophysectomized animal, the rate of lipid formation in the adrenal is reduced. ACTH had no effect on normal lipid-phosphorus concentration or specific activity but restored to normal both the concentration and specific activity of lipid-phosphorus in the adrenal of the hypophysectomized rat.

The specific activity of total ribonucleic acid - phosphorus (72) and the individual nucleotides (66) of the adrenal were decreased by hypophysectomy. A single intraperitoneal

injection of ACTH significantly increased the P^{32} uptake in the nucleotides of the adrenal in the hypophysectomied rat (66, 72) but had little effect on the same fractions in the adrenal of control rats.

A more recent report by Bransome and Reddy (74) showed that, although in vivo ACTH stimulation caused no significant difference in the mean deoxy-ribonucleic acid content of dog adrenal cortex, ribonucleic acid was increased in the canine cortical tissue. The greatest ribonucleic acid increase was in the microsomal fraction.

Exposure of normal rats to short periods in the cold has been reported to stimulate the incorporation of inorganic phosphate labelled with P^{32} into the acid soluble fractions (64, 69, 71, 75-77) and also the lipid-phosphorus and ribonucleic acid - phosphorus (77) of the adrenal. However, removal of the pituitary (64, 69) or suppression of adrenocorticotropin secretion by cortisone (75) abolishes this response to the cold. These investigators have assumed that endogenous ACTH, mobilized from the anterior pituitary in the acute reaction to stress, is a factor which increases incorporation of P^{32} into the various phosphorus - containing fractions of the adrenal gland.

Nicholls and Rossiter (76) found that, although in cold stressed animals there was increased uptake of P^{32} in the acid soluble fraction of the adrenal, there was no concomitant change in the phosphorus concentration. This effect was explained by an increase in the rate at which P^{32} passes from the extracellular fluid to the cellular portion of the gland. However, the increased activity found in the lipid and ribonucleic acid fractions (77)

was associated with a net increase in concentration of these compounds in the adrenal gland, indicating a net increase in synthesis of these phosphorus-containing organic compounds.

If rats were exposed to the cold for longer periods, the increase in P^{32} incorporation was biphasic (76). The first response was greater in magnitude and was maximal after two or three hours in the cold, followed by a return almost to normal by 24 hours. The second response did not occur until the animals had been maintained in the cold for several days. In experiments devised to ascertain the role of the thyroid gland in the adrenal response to cold (64) it was found that when the thyroid function was depressed by thiouracil, the increase in the incorporation of P^{32} into the acid soluble fractions of the adrenal, brought about by short exposures (three hours) in the cold, was unimpaired. The response after longer periods in the cold (eight days), although still present, was considerably decreased. These findings contribute strong support to the suggestion that the acute response to cold, as measured by increased uptake of P^{32}, by the adrenal gland is initiated by stimulation of the cortex by endogenous ACTH, released from the pituitary gland. The finding that the response in the phosphorus metabolism of the adrenal gland of animals exposed to the cold for eight days was greatly decreased when thyroid activity was depressed with thiouracil, indicates that part of the later response in the adrenal is, in part at least, dependent upon the activity of the thyroid gland. Rats, conditioned to the cold, did not elicit the great increases in the specific activities of adrenal acid soluble

fractions seen in normal animals, when both acclimatized and normal animals were subjected to severe cold (75). This observation is consistent with the view that the changes in phosphorus metabolism of the adrenal found after short exposures to cold are stimulated by endogenous release of ACTH in the early response to stressful stimuli.

Other conditions which stimulate the pituitary-adrenal system have been shown to increase the incorporation of P^{32} into the adrenal gland. In normal rats, the injection of adrenalin, histamine and pitressin caused a significant increase in relative specific activity of the adrenal inorganic phosphate, compared to that of the control rats receiving saline (78). However, when normal rats were treated with cortisone prior to the injection of these substances, there was no significant change. Similarly, the injection of these stimuli in hypophysectomized animals only slightly increased the mean relative specific activities.

C. TISSUE RESPIRATION OF THE ADRENAL GLAND.

Oxygen consumption by slices of adrenal cortex has been used as a criterion of cortical cellular metabolism by several groups of workers. An increase in oxygen utilization by the adrenal cortex has been observed after administration of ACTH *in vivo* (79) or *in vitro* (80-87).

Nichols and Little (81) found that slices of canine adrenal cortex consisting of the zona glomerulosa and a strip of zona fasiculata have a higher rate of oxygen consumption *in vitro* than do slices of zona fasiculata and zona reticularis. ACTH significantly stimulated the rate of oxygen consumption of both slices, the percentage increase in oxygen consumption being about equal for the two slices. Other investigators (83, 88) have observed a higher rate of oxygen uptake in the outer zones of adrenal gland than in the inner cortical tissue.

Sourkes and Heneage (88) and Gordon (89) observed that although adrenal homogenates appear to oxidize the Kreb's cycle intermediates at considerably faster rates than do slices, the respiration of adrenal slices is greater than that of homogenates.

Increased adrenal QO_2 values were reported in scorbutic guinea pigs (83), pregnant rats and in rats maintained on vitamin E deficient diet (90). When ACTH was added *in vitro* to the cortical tissue (83, 90) there was little increment in oxygen utilization. McKee and Walker (83) suggested that the reason for lack of augmentation of respiration, is that the gland is already maximally stimulated. Other non-specific chronic stressful stimuli, broken leg and vitamin A and D deficient diets (90) were reported to result in increased QO_2 of rat adrenal cortex.

Nichols, Davis and Green (91) reported that the rate of oxygen consumption of adrenal cortex slices from dogs five days after hypophysectomy and from dogs surgically traumatized (stressed) was normal and gave the usual increase in rate of oxygen consumption when ACTH was added *in vitro.*

In vitro addition of desoxycorticosterone to adrenal slices has been reported to have no effect (82), to inhibit (92) and to markedly increase (87) the endogenous respiration. Sourkes and Heneage (93) found that the adrenals of cortisone-treated rats showed a decreased endogenous respiration as well as greatly reduced rates of oxidation of various intermediates of the Kreb's cycle. In a further report (92) they found that the *in vitro* addition of cortisone or desoxycorticosterone inhibited the oxidation of substrates tested and, in addition, lowered the endogenous respiration. Desoxycorticosterone was the more potent inhibitor.

III EXPERIMENTAL

A. ANIMALS

Male guinea pigs were used in the first series. They were maintained on lettuce, carrots, dog food pellets and water ad libitum.

Male albino rats of the Sprague-Dawley strain were used in all subsequent series. Normal intact animals were maintained on dog food pellets and water ad libitum.

Rats hypophysectomized by the transpharyngeal route were obtained from Hormone Assay Laboratories#. Hypophysectomized rats were maintained on a diet of oranges, carrots, potatoes, brown bread, oatmeal, milk and water ad libitum.

Adrenalectomy was performed by the dorsal route while the animals were under light ether anesthesia. Adrenalectomized rats received drinking water containing one percent sodium chloride ad libitum and dog food pellets.

B. INJECTIONS

Adrenocorticotropic Hormone (ACTH, Parke, Davis and Co., Ltd.) was administered by intraperitoneal injection to both intact and hypophysectomized rats and intact guinea pigs. The amount of ACTH injected was 4 milligrams per 100 grams body weight as a single dose 24 hours before sacrificing. The amount of ACTH administered was the same as that employed by others (5, 65).

#Hormone Assay Lab. Inc., Chicago, Ill.

Desoxycorticosterone acetate (DCA)@ was prepared as a 0.6 per cent suspension in sesame oil and was administered by intraperitoneal injection to both intact and adrenalectomized rats. The amount of DCA injected was 6 milligrams as a single dose (acute experiments) given 24 hours before sacrifice, and 3 milligrams as a daily dose (chronic experiments) which was administered for a period of 8 days. The last dose was administered 24 hours before the animal was killed. The dose of DCA administered in the acute and chronic experiments had been used previously in this laboratory (5).

Radioactive phosphorus (P^{32})# was administered by intraperitoneal injection to the animals of both the test and control groups. Guinea pigs received 200 microcuries P^{32} 16 hours before killing and rats received 50 microcuries P^{32} 24 hours before killing. The animals were weighed at the time of the isotope injection and fasted until sacrificed.

C. REMOVAL OF TISSUES

Guinea pigs were killed by a sharp blow on the head. A vertical incision was made up the abdomen to the diaphragm. The animal was inverted over a 20 ml. beaker containing 0.1 ml. Heparin* and a blood sample was collected. The blood sample was transferred to a 15 ml. centrifuge tube and immediately centrifuged at 2000 r.p.m. for approximately 20 minutes. The adrenal and prostate glands were quickly removed, placed in petri dishes lined with moist filter paper, and stored in a moist, cold (2 - 5° C) chamber.

@ Supplied by Ciba Co. Ltd., Montreal

as H_3PO_4 in HCl obtained from Atomic Energy of Canada, Ltd.,

* Lipo-Heparin, 1000 U.S.P. Units per cc

(Riker Pharmaceuticals Co., Ltd.)

Rats were killed by decapitation. In order to obtain sufficient adrenal tissue, at least three rats were sacrificed at one time. Each rat was inverted over a separate 20 ml. beaker and a blood sample collected and centrifuged in the same manner as described for the guinea pig. A vertical incision was made up the abdomen to the diaphragm and the adrenal glands and prostate gland were quickly excised. The prostate was separated into the dorsolateral and ventral portions. The tissues were pooled and stored as described above.

D. DETERMINATION OF TISSUE RESPIRATION

In order to measure the respiration of tissues in contact with oxygen, it is necessary to have the samples suspended in such a manner as to ensure maximal contact of the tissue with the gas. A method that meets this requirement was proposed by Huston and Martin (94) in which specially-designed vessels are used (95). The tissue slices are carefully spread out on fiber-glass mats to permit ready contact of gas with both sides of the slice, then the mats are placed on removable trays in the wide-mouth Huston-Martin flasks. The Huston-Martin technique has been successfully applied in various pharmacological studies in this laboratory (96, 97).

1. Preparation of tissue samples

The adrenals were cleaned of adherent fat and sliced thinly with a razor blade. The slices were carefully spread out on tared fibre-glass mats, which were kept in moist petri dishes in the refrigerated cabinet until all sections were ready for weighing. Two tissue slice preparations were obtained from each guinea pig adrenal. The remaining portion of each

adrenal was saved for determination of phosphorus and radioactivity. Four guinea pig adrenal samples for determination of tissue respiration were obtained from one animal. The slices of rat adrenal were pooled and one sample was obtained for determination of tissue respiration.

The prostate was cleaned of adherent fat and spread evenly on tared fibre-glass mats. The mats were stored as described above. Four guinea pig prostate samples for determination of tissue respiration were obtained from each animal. The remaining guinea pig prostate tissue was saved for determination of phosphorus and radioactivity. The rat prostate portions were pooled. One sample of dorsolateral prostate and one sample of ventral prostate was obtained for determination of tissue respiration.

2. Apparatus and Method

After weighing the tissue samples on a Gram-atic balance, the samples were placed on removable trays in the Huston-Martin flasks and attached to standard Warburg manometers by a glass adaptor. After attachment to the manometers, the flasks were placed in the constant temperature water bath at 37.9° C and flushed with oxygen for two minutes. Then all ground glass connections were thoroughly tightened and approximately ten minutes was allowed for thermal equilibrium. The oxygen consumption was determined by the direct method of Warburg using a gas phase of oxygen. Readings were taken at ten minute intervals for eighty minutes. No longer than twenty-five minutes elapsed from the time the animal was killed until the flasks were placed in the water bath.

Guinea pig prostate tissue samples were placed in flasks of about 7 ml. capacity. All other tissue samples were placed in flasks of about 12 ml. capacity. Carbon dioxide was absorbed by potassium hydroxide which was absorbed on a piece of filter paper on the bottom of the flask. 0.1 ml. 10% potassium hydroxide was used in the smaller flasks and 0.2 ml. 10% potassium hydroxide in the larger flasks. 0.4 ml. Krebs Ringer Phosphate (98) (KRP) was placed in the removable tray of the smaller flasks, 1.0 ml. KRP in the tray of the larger flasks. The flasks were prepared as described and warmed to approximately 37° C in a water bath before the tissue samples were placed in them.

3. Calculation of Results

Warburg manometers record changes in pressure of gas in the flask. The flask constant, coupled with the weight of the tissue is used to determine a standardized QO_2. The QO_2 used in this investigation expresses ml. of oxygen consumed per gram of tissue (wet weight) per hour. Since the rate of respiration in artificial media declines with time, the QO_2 value for zero time must be obtained by straight line extrapolation of the rates during the experimental period. The rate of respiration has been depressed by the cold during the operation procedure and returns to a maximum at the conclusion of thermal equilibrium. This rate of respiration is therefore the closest approximation to that *in situ*.

E. SEPARATION OF ACID SOLUBLE PHOSPHORUS

Phosphorus is unique among the inorganic nutritional elements in that it is involved in a major mechanism for the storage and mobilization of energy, namely phosphorylation. The metabolism

of phosphorus is an indication of the metabolism and energy consumption in a tissue. Inorganic phosphates and ester phosphates, which play an important part in energy-donating metabolism, are soluble in tricloroacetic acid (TCA).

After centrifugation of the blood sample, two 0.5 ml. aliquots of guinea pig plasma were removed. One 0.3 ml. aliquot of rat plasma was removed from each blood sample. The rat plasma samples were pooled. The plasma samples were extracted three times with 1.0 ml. cold 10% TCA and the combined supernatants were diluted to 10.0 ml. with demineralized distilled water.

The portion of each guinea pig adrenal remaining after samples had been taken for determination of tissue respiration was weighed and homogenized in 1.0 ml. 10% TCA using a glass homogenizer of the Potter and Elvehjem type. The homogenizer tube and contents were centrifuged and the supernatant removed. Homogenization and centrifugation were repeated two more times. The three supernatant aliquots were combined and diluted to 10.0 ml. with demineralized distilled water.

Two samples of the remaining guinea pig prostate portion were weighed and carried through the same homogenization procedure as described for the adrenal.

After the termination of the tissue respiration study, the mats holding the rat tissues were removed from the flasks and placed in the homogenizer tubes. Homogenization, centrifugation and collection of supernatants was carried out as described above.

F. QUANTITATIVE DETERMINATION OF PHOSPHORUS

Duplicate 1.0 ml. aliquots of the cold TCA soluble extracts were taken for phosphorus determination. Four samples of adrenal, prostate and blood were obtained for each guinea pig sacrificed. Two samples of adrenal, dorsolateral and ventral prostates and blood were obtained for each group of rats sacrificed.

The 1.0 ml. aliquots of TCA soluble extract were wet ashed with 0.5 ml. of a mixture of 3 parts H_2SO_4 and 2 parts 60% $HClO_4$ in 10 or 30 ml. Kjeldahl flasks on an Electrothermal Kjeldhal Apparatus. The solution was ashed approximately 10 minutes, until the solution had turned a light yellow color and returned to colorless. The cooled, ashed material was then diluted with 8.0 ml. of demineralized distilled water and neutralized with concentrated ammonium hydroxide, using two drops of bromothymol blue as indicator. The end point was reached when one drop of the base turned the yellow solution to blue.

A blank was prepared by diluting 3.0 ml. of 10% TCA to 10.0 ml. with demineralized distilled water. Standard solutions were prepared containing 5, 10 or 20 micrograms phosphorus per ml. (as KH_2PO_4). One 1.0 ml. aliquot of the blank and each of the standard phosphorus solutions were wet ashed along with the tissue samples as described above.

One ml. of an acid molybdate color reagent (99) was added to each of the neutralized solutions from the wet ashing procedure and the solution was placed in a boiling water bath for thirty minutes. The solution was then removed, cooled and the absorbance measured in a Beckman Model B Spectrophotometer at 780 mμ. Distilled water was used as the reference solution.

The value of the blank was subtracted from each reading before the amount of phosphorus contained in each fraction was calculated. The optical densities of the standard solutions were plotted against micrograms phosphorus. The Lambert-Beer law was satisfied over the range investigated. This method for determination of phosphorus had been previously used in this laboratory (100). The phosphorus concentration of the samples was determined by a direct comparison with the corrected optical densities of the phosphorus standards. The concentration of phosphorus in each tissue sample was then determined $\frac{\mu g \text{ phosphorus} \times \text{dilution factor}}{\text{mg. wet weight of tissue}}$.

Comparable results were obtained in preliminary experiments when the phosphorus was determined in standard solutions which had not been wet ashed and neutralized and in standard solutions which were carried through the ashing procedure described above. This indicated that phosphorus was not lost to any appreciable extent during wet ashing and that the light yellow color of the bromothymol blue in acid solution did not interfere with the measurement of the blue color produced by the phosphomolybdate.

G. DETERMINATION OF RADIOACTIVITY

The radioactivity of the samples was estimated in an M-6 liquid Geiger-Müller counting tube (20th Century Electronics) attached to a decade scaler (Tracerlab, Inc., Boston, Mass.) It was convenient to use the colored solution prepared for the phosphorus estimation directly in the liquid counter. All counts were corrected for background, differences in the standard count, and for radioactive decay.

Counting error

The standard error of a counting rate $n_s - n_b$ is

$$\pm \sqrt{\left(\frac{\sqrt{N_s}}{t_s}\right)^2 + \left(\frac{\sqrt{N_b}}{t_b}\right)^2}$$

where N_s = total sample count recorded

t_s = total sample counting time

N_b = total background count recorded

t_b = total background count time

$n_s = \frac{N_s}{t_s}$ = sample counting rate

$n_b = \frac{N_b}{t_b}$ = background counting rate

All samples were counted for 3 minutes and the lowest uncorrected count recorded was 200 counts per 3 minutes. Background, which was counted for 10 minutes, was never more than 180 counts per 10 minutes. Under these conditions the standard error of the counting rate was 48.7 $\pm$ 3.8 counts per minute. The percentage standard error was 7.8%. For most samples, the net counting rate was greater than 48 counts per minute; therefore, the percentage standard error was less than 7.8%.

P^{32} standards

In order to correct for variations in the injected dose from experiment to experiment, the same measured volume of the solution of P^{32} used for the injection was taken for the preparation of a standard. This volume was diluted to 50 ml. with N/10 HCl in a volumetric flask. Triplicate 20 lambda aliquots were dried on planchettes and counted with an end-window Geiger-Müller counting tube (Tracerlab). The average counting rate of the first dose injected in a series was assigned a value of 100 per cent. Subsequent injections in the series were corrected to this standard dose. A simulated P^{32} standard (Tracerlab) was also counted to correct for mechanical variations within the counting equipment.

H. DEFINITION OF TERMS

The specific activity (S.A.) of a sample is defined as the number of counts per minute per microgram of phosphorus.

$$\text{i.e., S.A.} = \frac{\text{counts per minute}}{\text{micrograms of phosphorus in sample}}$$

Since a constant amount of P^{32} was injected, regardless of the size of the animal, it was necessary, when plasma samples from different animals were to be compared, to correct the specific activity for differences in dilution. The specific activity of the plasma inorganic phosphorus obtained for a particular animal was multiplied by the body weight, to give a value (corrected specific activity) independent of animal size.

i.e., corrected S.A. = S.A. of plasma inorganic phosphorus x body weight.

The relative specific activity (RSA) of a sample is defined as the S.A. of a sample relative to the corrected S.A. For convenience this figure was multiplied by 10^3.

$$\text{i.e., RSA} = \frac{\text{S.A. of sample}}{\text{corrected S.A.}} \times 10^3$$

The mean QO_2, phosphorus concentration, specific activity, and relative specific activity of each tissue investigated was determined. Any difference from normal values noted was tested for significance by the Student's "t" test (101). The probability of 0.05 was selected as the point of significance. The letter "S" signifies that the difference in means between a treated and non-treated group is statistically significant.

IV OBSERVATIONS

The experimental work was divided into two parts. Part A was a study of the effect of hypophysectomy and the administration of ACTH on the QO_2, phosphorus concentration and P^{32} incorporation of selected tissues. Part B was a similar study of the effect of adrenalectomy and the administration of DCA. The results are summarized in the following sections. The detailed records are presented in table form in the Appendix. The results are recorded for the following tissues:- plasma, adrenal gland, dorsolateral prostate and ventral prostate.

Part A HYPOPHYSECTOMY AND ACTH

The ACTH experiments were conducted as follows:-

Series I	Intact guinea pigs
	ACTH-treated intact guinea pigs
Series II	Intact rats
	ACTH-treated intact rats
Series III	Intact rats
	Hypophysectomized (4 - 20 days) rats
	ACTH-treated hypophysectomized (4 - 20 days) rats
Series IV	Intact rats
	ACTH-treated intact rats
	Hypophysectomized (4 days) rats
	ACTH-treated hypophysectomized (4 days) rats

1. Plasma (Tables I and II, Figure I)

A statistical comparsion of the effects of hypophysectomy and the administration of ACTH on the phosphorus concentration and P^{32} uptake in blood plasma is presented in Tables I and II. A graphic summary of the results is shown in Figure I.

The plasma-P concentration in 4 - 20 day hypophysectomized rats was significantly decreased from normal. A similar trend in the plasma-P concentration was seen in the 4 day hypophysectomized animals. This reduction was not significant ($P \geq 0.15$). Although a single injection of ACTH raised the plasma-P content in both normal and hypophysectomized animals, these increases were not significant. However, ACTH increased the plasma-P concentration in 4 - 20 day hypophysectomized rats sufficiently so that the level, although lower than normal, was not significantly different from the normal level.

The plasma-P specific activity in both the 4 - 20 day and the 4 day hypophysectomized rats was significantly higher than normal. When the plasma-P specific activity was corrected for body weight the corrected specific activity in the 4 - 20 day hypophysectomized rats was significantly higher than normal. Although the plasma-P corrected specific activity in 4 day hypophysectomized rats was higher than normal, this increase was not statistically significant.

The administration of ACTH to normal guinea pigs significantly decreased the plasma-P specific activity. However,

the corrected specific activity, although lower than normal, was not significantly different. A single injection of ACTH had little effect on plasma-P specific activity in intact rats or in hypophysectomized rats.

2. Adrenal (Tables III and IV, Figure II)

The mean adrenal QO_2 was markedly reduced in both the 4 - 20 day and 4 day hypophysectomized groups. Administration of ACTH significantly increased the adrenal QO_2 in intact guinea pigs and rats and in 4 day hypophysectomized rats. The increased adrenal QO_2 in ACTH-treated 4 - 20 day hypophysectomized rats approached statistical significance ($0.1 > P > 0.05$). Table IV shows that the mean adrenal QO_2 of the 4 day hypophysectomized and ACTH-treated hypophysectomized rats was greater than the mean QO_2 of the 4 - 20 day hypophysectomized group similarly treated.

A single injection of ACTH significantly increased the adrenal-P concentration in intact guinea pigs but had little effect in normal or in hypophysectomized rats.

A significant increase in adrenal-P concentration was observed in both the 4 - 20 day and 4 day hypophysectomized groups.

The specific activity of ACTH-treated guinea pig adrenal-P, although lower than normal, was not significantly different. This effect may have been a reflection of the decreased plasma-P specific activity of the ACTH-treated guinea pigs (Table I). The adrenal-P relative specific activity of ACTH-treated guinea pigs was significantly greater than normal. Administration of ACTH to intact rats significantly increased both the specific

activity and relative specific activity of adrenal-P.

The adrenal-P specific activity of 4 - 20 day hypophysectomized rats was not significantly different from normal, an effect which probably reflected the increased plasma-P specific activity (Table II). Riedel et al (60) has shown that the adrenal-P specific activity increases with time after hypophysectomy, but when the adrenal-P specific activity relative to plasma-P specific activity is compared between normal and hypophysectomized rats, the adrenal-P relative specific activity of hypophysectomized rats remains at a constant level below normal.

In 4 day hypophysectomized rats, the adrenal-P specific activity was significantly less than normal. The adrenal-P relative specific activity was significantly less than normal in both the 4 - 20 day and 4 day hypophysectomized groups.

Twenty-four hours after a single injection of ACTH, the adrenal-P specific activity and relative specific activity was significantly elevated above normal in both the 4 - 20 day and the 4 day hypophysectomized rats. There was no significant difference between the adrenal-P specific activity and relative specific activity of ACTH-treated hypophysectomized and ACTH-treated normal rats in Series IV.

3. Dorsolateral Prostate (Table V, Figure III)

The administration of ACTH had no significant effect on any measurements carried out on the dorsolateral prostate in either intact or hypophysectomized rats.

Hypophysectomy significantly reduced the dorsolateral prostate QO_2 in the 4 - 20 day Series but had no effect in the 4 day Series.

The dorsolateral prostate-P concentration was significantly decreased in both hypophysectomized groups.

Both the specific activity and the relative specific activity of dorsolateral prostate-P were increased in the 4 - 20 day hypophysectomized rats. A similar trend was noted in the 4 day hypophysectomized rats but the increases were not significantly different from normal.

4. Ventral Prostate (Tables VI and VII, Figure IV)

Administration of ACTH significantly increased the guinea pig prostate QO_2 but had little effect on ventral prostate QO_2 in either intact rats or hypophysectomized rats.

Hypophysectomy significantly reduced the ventral prostate QO_2 in the 4 - 20 day Series but had no effect in the 4 day Series.

Hypophysectomy significantly increased the ventral prostate-P concentration. Administration of ACTH to intact rats (Series IV) significantly increased the ventral prostate-P concentration. In other experiments (Series II - IV) administration of ACTH had no effect on the ventral prostate-P concentration in either intact or hypophysectomized animals.

Administration of ACTH increased guinea pig prostate relative specific activity (Series I), but significantly decreased intact rat ventral prostate-P specific activity and relative specific activity in Series IV. In other experiments (Series II - IV) administration of ACTH did not have a significant effect on ventral prostate-P specific activity or relative specific activity in either intact or hypophysectomized rats.

Hypophysectomy significantly increased the ventral prostate-P specific activity and relative specific activity in the 4 - 20 day Series. In contrast, a slight decrease in the 4 day Series was noted. ACTH treatment, however, lowered the ventral prostate-P relative specific activity to a value which was significantly lower than normal in the 4 day hypophysectomized rats.

Table I

PLASMA - Effect of the Administration of ACTH on Phosphorus Concentration and P^{32} Incorporation

Group of Animals	Body Weight in Grams	Phosphorus Content µg./ml.	Sig.	Specific Activity	Corrected Specific Activity	Sig.
Series I (guinea pigs)						
Intact	662 (9) *	84 ± 25 (27)		76.8 ± 33.1 (23)	57.3 ± 32.6 (6)	
Intact + ACTH	736 (9)	97 ± 25 (30)		41.9 ± 9.1 (20)	30.1 ± 7.4 (6)	
Series II (rats)						
Intact	266 (15)	120 ± 25 (14)		26.2 ± 7.2 (14)	66.3 ± 15.7 (7)	
Intact + ACTH	263 (8)	125 ± 40 (12)		27.3 ± 6.7 (12)	71.7 ± 14.1 (6)	

* Figures in parenthesis indicate number of determinations

Table II

PLASMA - Effect of Hypophysectomy and the Administration of ACTH on Phosphorus Concentration and P^{32} Incorporation

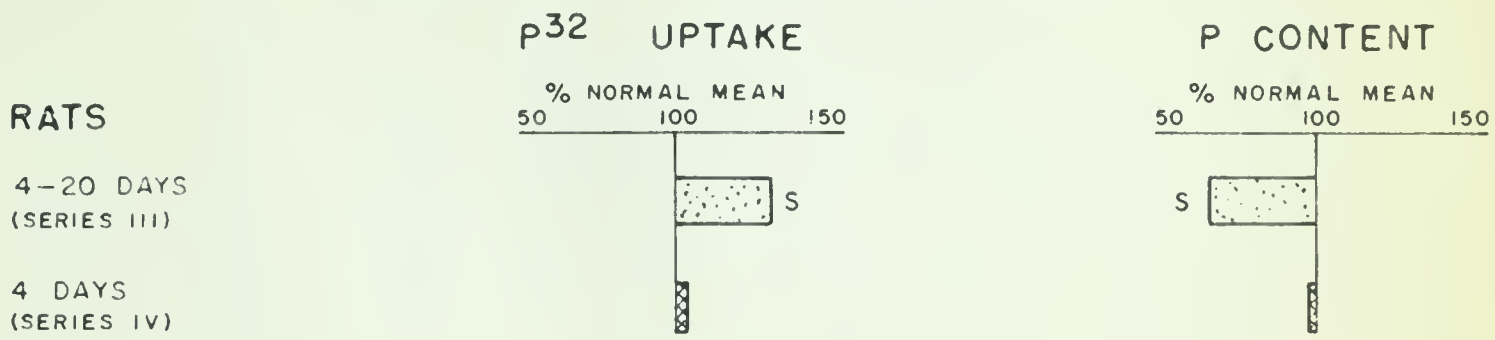
Group of Animals	Body Weight in Grams	Phosphorus Content µg./ml.	Sig.	Specific Activity	Corrected Specific Activity	Sig.
Series III (rats)						
Intact	232 (11) *	78 ± 6 (20)	S	23.2 ± 5.7 (20)	53.0 ± 7.5 (10)	S
Hypophysectomized (4 - 20 days)	142 (13)	68 ± 14 (26)		50.8 ± 8.3 (26)	71.8 ± 9.4 (13)	S
Hypophysectomized + ACTH (4 - 20 days)	143 (12)	74 ± 21 (24)		53.2 ± 11.2 (24)	76.2 ± 14.7 (12)	
Series IV (rats)						
Intact	170 (6)	87 ± 7 (12)		31.6 ± 3.4 (12)	53.5 ± 5.2 (6)	
Intact + ACTH	168 (6)	84 ± 4 (10)		30.7 ± 3.4 (10)	52.3 ± 7.7 (5)	
Hypophysectomized (4 days)	147 (8)	85 ± 12 (14)		38.0 ± 6.3 (14)	55.9 ± 8.4 (7)	
Hypophysectomized + ACTH (4 days)	149 (8)	88 ± 15 (16)		37.8 ± 4.3 (16)	56.2 ± 5.9 (8)	

* Figures in parenthesis indicate number of determinations

FIGURE 1

P L A S M A

EFFECT OF HYPOPHYSECTOMY



EFFECT OF ACTH

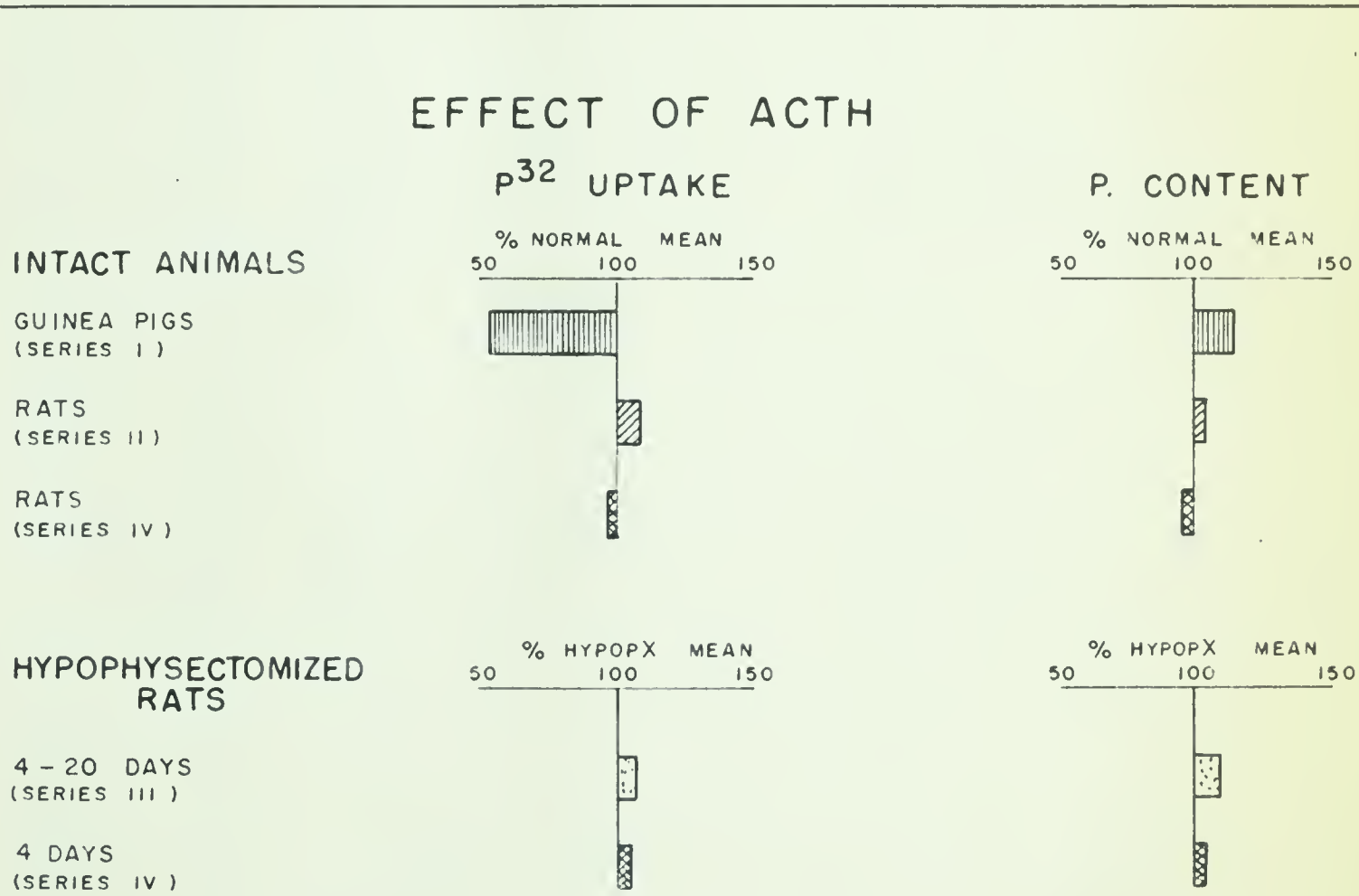


Table III

ADRENAL - Effect of the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

Group of Animals	QO_2 ml.O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Series I (guinea pigs)							
Intact	1.77 ± 0.21 (34)*	S	1.39 ± 0.11 (22)	S	47.2 ± 16.5 (18)	876 ± 591 (18)	S
Intact + ACTH	2.00 ± 0.20 (24)		1.60 ± 0.17 (31)		39.7 ± 5.1 (19)	1445 ± 389 (19)	
Series II (rats)							
Intact	2.21 ± 0.40 (15)	S	1.41 ± 0.45 (14)		21.3 ± 4.2 (14)	334 ± 90 (14)	S
Intact + ACTH	2.89 ± 0.19 (8)		1.38 ± 0.67 (14)		34.0 ± 5.3 (14)	490 ± 142 (12)	

* Figures in parenthesis indicate number of determinations

Table IV

ADRENAL - Effect of Hypophysectomy and the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

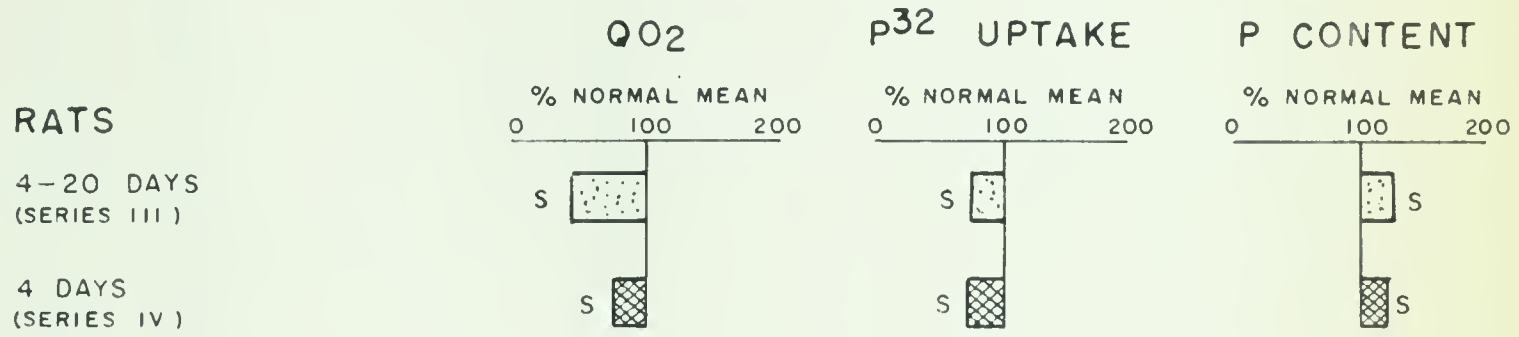
Group of Animals	QO_2 ml.O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Series III (rats)							
Intact	2.81 ± 0.23 (11) *	S	1.36 ± 0.24 (20)	S	19.4 ± 6.7 (20)	364 ± 109 (20)	S
Hypophysectomized (4 - 20 days)	1.13 ± 0.19 (13)	S	1.70 ± 0.41 (26)	S	20.2 ± 8.6 (26)	278 ± 105 (26)	S
Hypophysectomized + ACTH (4 - 20 days)	1.36 ± 0.36 (12)		1.78 ± 0.57 (20)		37.2 ± 12.8 (20)	519 ± 181 (20)	S
Series IV (rats)							
Intact	2.64 ± 0.27 (6)	S	1.16 ± 0.17 (11)	S	22.3 ± 1.3 (11)	407 ± 46 (11)	S
Intact + ACTH	3.14 ± 0.21 (6)	S	1.29 ± 0.15 (10)	S	33.7 ± 7.1 (10)	656 ± 159 (10)	S
Hypophysectomized (4 days)	1.95 ± 0.15 (8)	S	1.39 ± 0.14 (14)	S	16.5 ± 4.0 (14)	294 ± 58 (14)	S
Hypophysectomized + ACTH (4 days)	2.38 ± 0.08 (8)	S	1.36 ± 0.20 (16)	S	32.5 ± 7.6 (16)	576 ± 112 (16)	S

* Figures in parenthesis indicate number of determinations

FIGURE II

ADRENAL

EFFECT OF HYPOPHYSECTOMY



EFFECT OF ACTH

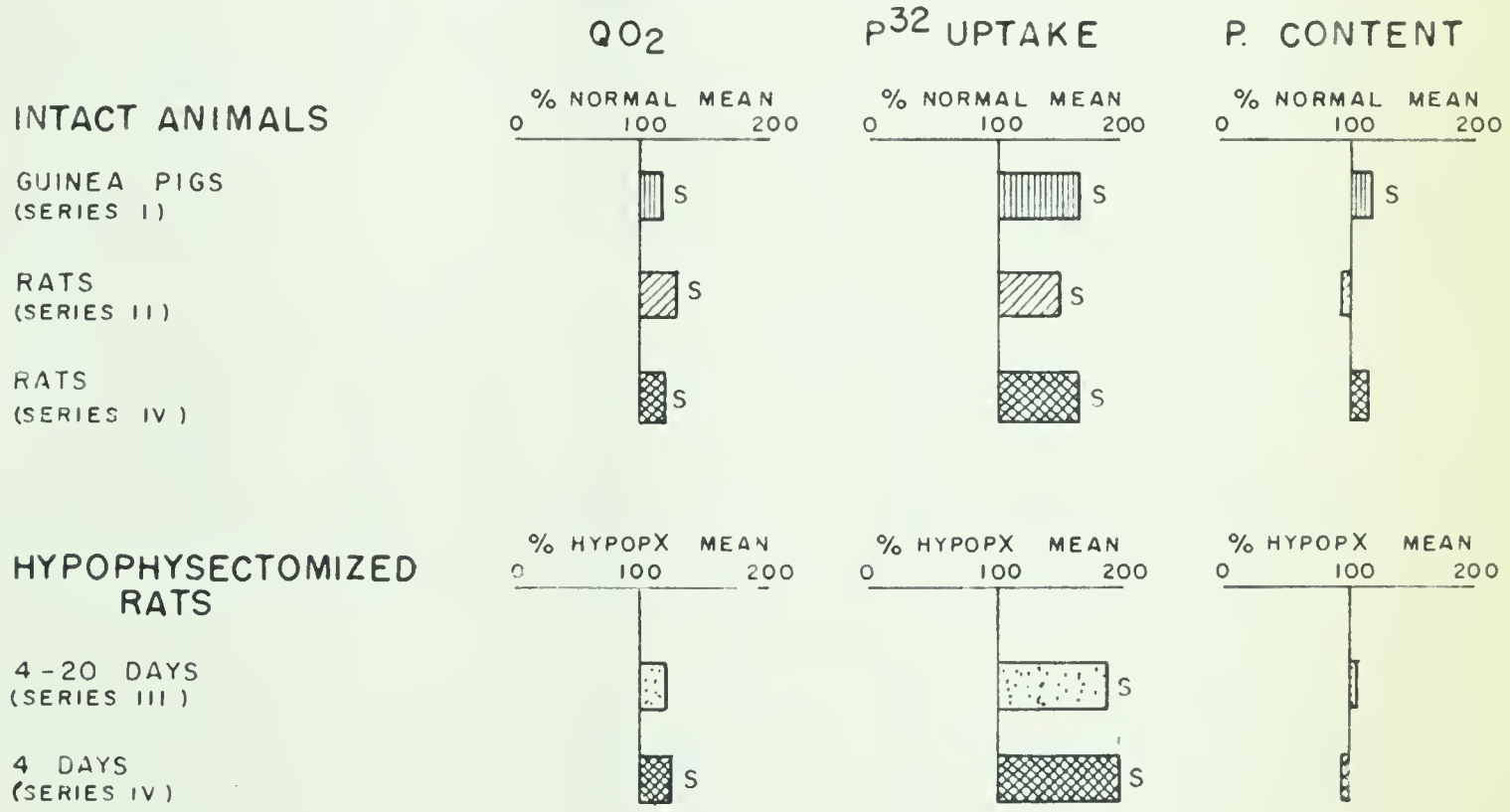


Table V

DORSOLATERAL PROSTATE - Effect of Hypophysectomy and the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

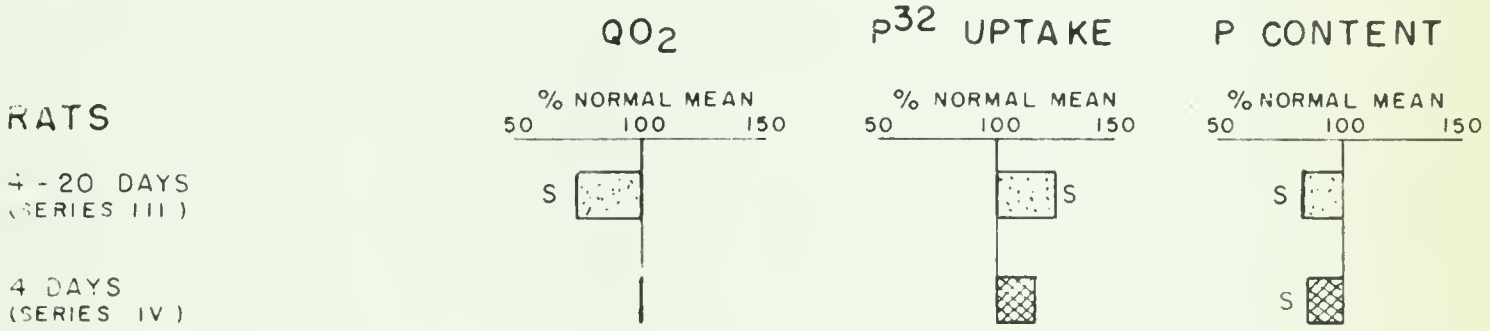
Groups of Animals	QO_2 ml.O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Series III (rats)							
Intact	0.97 ± 0.12 (11) *	S	1.87 ± 0.26 (19)	S	13.1 ± 3.2 (19)	254 ± 77 (19)	S
Hypophysectomized (4 - 20 days)	0.72 ± 0.08 (13)	S	1.62 ± 0.46 (26)	S	22.8 ± 9.8 (26)	317 ± 118 (26)	S
Hypophysectomized + ACTH (4 - 20 days)	0.75 ± 0.17 (12)		1.45 ± 0.36 (24)		27.3 ± 7.9 (22)	379 ± 109 (22)	
Series IV (rats)							
Intact	0.93 ± 0.10 (6)		2.05 ± 0.27 (12)	S	15.1 ± 1.9 (12)	283 ± 26 (12)	
Intact + ACTH	0.96 ± 0.11 (6)		2.11 ± 0.22 (10)	S	15.8 ± 2.8 (10)	309 ± 75 (10)	
Hypophysectomized (4 days)	0.93 ± 0.14 (8)		1.81 ± 0.16 (14)		18.8 ± 8.5 (14)	331 ± 111 (14)	
Hypophysectomized + ACTH (4 days)	0.92 ± 0.13 (8)		1.79 ± 0.16 (16)	S	18.0 ± 6.2 (16)	322 ± 106 (16)	

* Figures in parenthesis indicate number of determinations

FIGURE III

DORSOLATERAL PROSTATE

EFFECT OF HYPOPHYSECTOMY



EFFECT OF ACTH

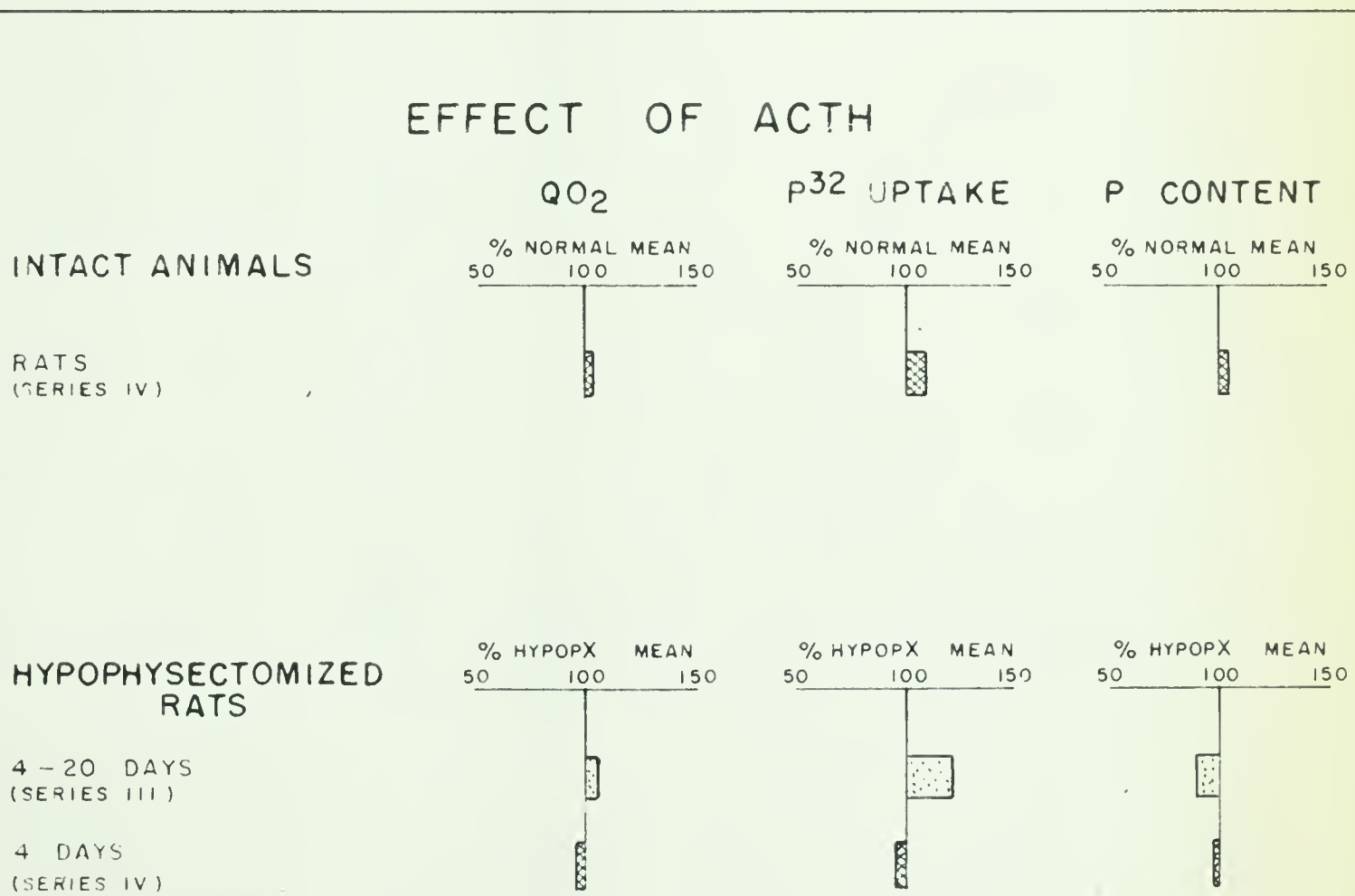


Table VI

VENTRAL PROSTATE - Effect of the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

Group of Animals	QO_2 ml.O_2/GM./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Series I (guinea pigs)							
Intact	0.37 ± 0.13 (35) *	S	0.93 ± 0.16 (22)		23.7 ± 6.0 (18)	433 ± 139 (18)	S
Intact + ACTH	0.43 ± 0.10 (35)		1.03 ± 0.21 (35)		20.9 ± 3.8 (22)	699 ± 139 (22)	
Series II (rats)							
Intact	1.15 ± 0.15 (15)		1.05 ± 0.25 (12)		20.0 ± 3.3 (12)	304 ± 53 (12)	
Intact + ACTH	1.25 ± 0.15 (8)		0.93 ± 0.21 (14)		21.9 ± 3.3 (14)	306 ± 64 (12)	

* Figures in parenthesis indicate number of determinations

Table VII

VENTRAL PROSTATE - Effect of Hypophysectomy and the Administration of ACTH on

QO_2, Phosphorus Concentration and P^{32} Incorporation

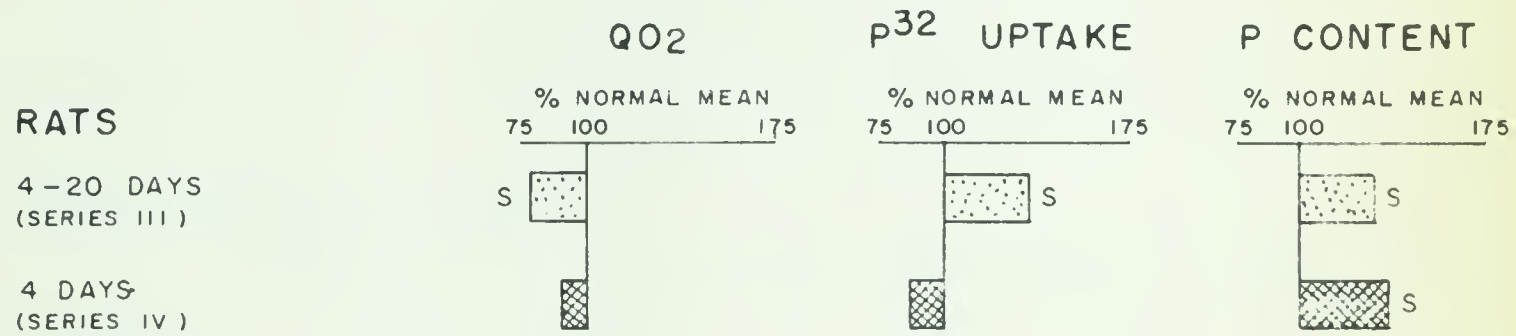
Group of Animals	QO_2 ml.O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Series III (rats)							
Intact	1.17 ± 0.12 (10) *	S	0.84 ± 0.20 (20)	S	16.8 ± 6.2 (20)	319 ± 116 (20)	S
Hypophysectomized (4 - 20 days)	0.91 ± 0.15 (13)	S	1.10 ± 0.26 (24)	S	31.8 ± 15.8 (24)	432 ± 190 (24)	S
Hypophysectomized + ACTH (4 - 20 days)	0.98 ± 0.17 (12)	S	1.14 ± 0.31 (23)	S	33.0 ± 16.8 (23)	426 ± 157 (23)	S
Series IV (rats)							
Intact	1.04 ± 0.09 (6)		0.66 ± 0.09 (12)	S	22.0 ± 4.4 (12)	412 ± 75 (12)	S
Intact + ACTH	0.98 ± 0.08 (6)		0.79 ± 0.14 (10)	S	17.0 ± 3.2 (10)	329 ± 66 (10)	S
Hypophysectomized (4 days)	0.96 ± 0.12 (8)		0.89 + 0.17 (14)	S	20.4 ± 6.1 (14)	359 ± 70 (14)	S
Hypophysectomized + ACTH (4 days)	0.97 ± 0.15 (8)		0.93 ± 0.21 (16)	S	18.2 ± 5.9 (16)	323 ± 91 (16)	S

* Figures in parenthesis indicate number of determinations

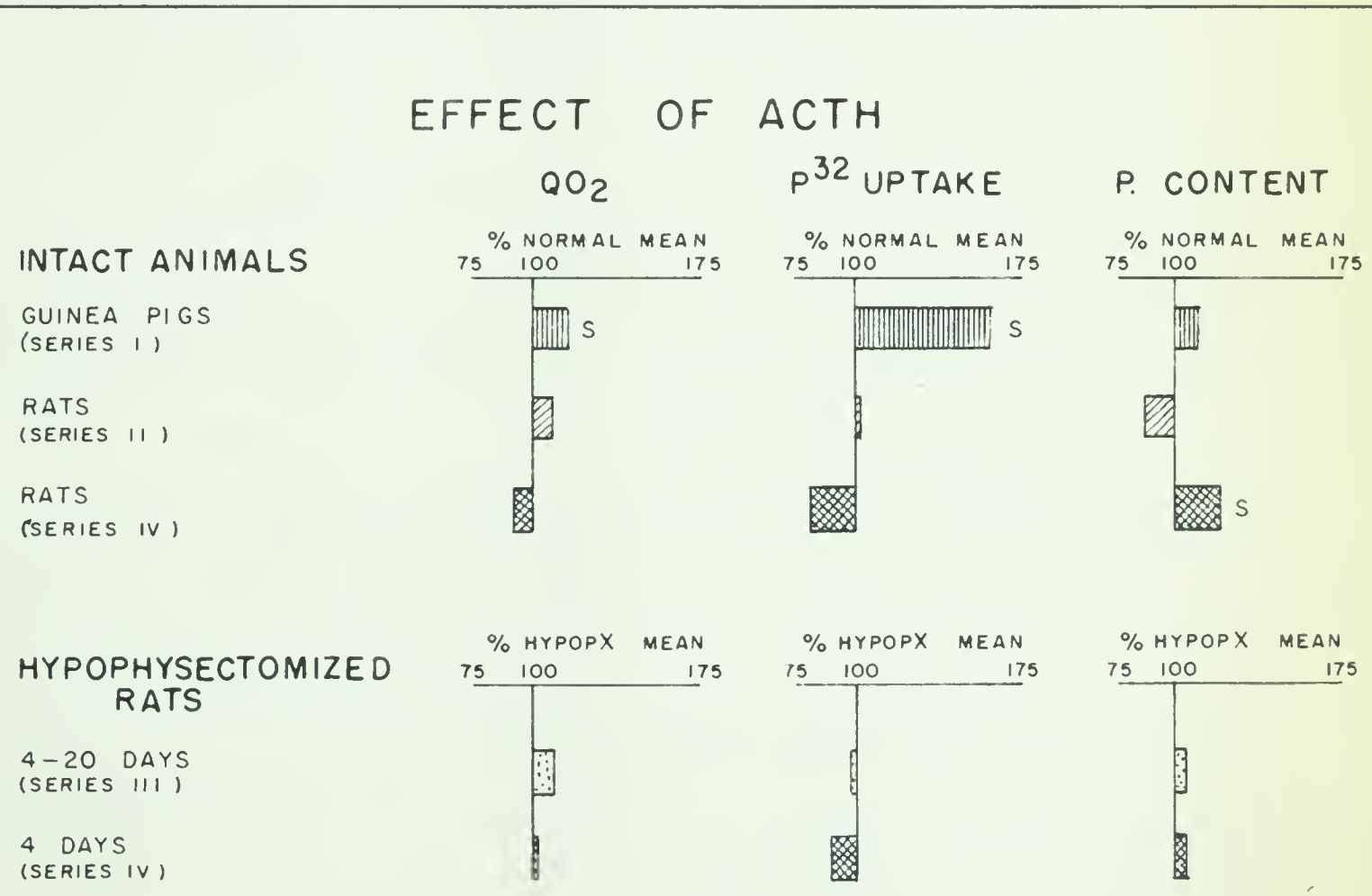
FIGURE IV

VENTRAL PROSTATE

EFFECT OF HYPOPHYSECTOMY



EFFECT OF ACTH



Part B ADRENALECTOMY AND DCA

The DCA experiments were conducted as follows:-

DCA (acute)	Intact rats
	DCA-treated intact rats
DCA (chronic)	Intact rats
	DCA-treated intact rats
	Adrenalectomized rats
	DCA-treated adrenalectomized rats

1. Plasma (Table VIII, Figure V)

DCA (acute) had little effect on plasma-P concentration or specific activity.

DCA (chronic) treatment increased the plasma-P concentration in intact animals but had little effect in adrenalectomized animals. Adrenalectomy increased the plasma-P concentration.

Adrenalectomy significantly increased the plasma-P specific activity and corrected specific activity. DCA (chronic) treatment of adrenalectomized rats reduced the plasma-P specific activity to normal and lowered the corrected specific activity toward normal. DCA (chronic) slightly depressed the plasma-P specific activity in normal animals.

2. Adrenal (Table IX, Figure VI)

DCA (acute) significantly increased the adrenal QO_2 but no other changes were observed.

DCA (chronic) slightly depressed the adrenal QO_2 and relative specific activity. The depression in both cases approached significance ($0.10 > p > 0.05$). The adrenal-P concentration was unchanged by DCA (chronic).

3. Dorsolateral Prostate (Table X, Figure VII)

No changes were observed in the dorsolateral prostate after a single injection of DCA.

Adrenalectomy decreased the dorsolateral prostate QO_2. DCA (chronic) decreased the dorsolateral prostate QO_2 in normal rats but had no effect in adrenalectomized rats.

Neither the dorsolateral prostate-P concentration nor the specific activity was changed by adrenalectomy or by DCA (chronic) in either normal or adrenalectomized rats.

Adrenalectomy significantly reduced the dorsolateral prostate-P relative specific activity. DCA (chronic) had little effect on dorsolateral prostate-P relative specific activity in either normal or adrenalectomized rats.

4. Ventral Prostate (Table XI, Figure VIII)

No changes were observed in the ventral prostate after a single injection of DCA.

The ventral prostate QO_2 was unaffected by adrenalectomy or by DCA (chronic) in either normal or adrenalectomized rats.

Adrenalectomy significantly increased the ventral prostate - P concentration. DCA (chronic)significantly increased the ventral prostate - P concentration in normal but reduced the phosphorus concentration in adrenalectomized rats so that the level was no longer significantly different from normal.

Adrenalectomy significantly increased the ventral prostate - P specific activity but the relative specific activity was not significantly different from normal.

DCA (chronic) had no significant effect on ventral prostate - P specific activity or relative specific activity in either normal or adrenalectomized rats.

Table VIII

PLASMA - Effect of Adrenalectomy and the Administration of DCA on Phosphorus Concentration and P^{32} Incorporation

Group of Animals	Body Weight in Grams	Phosphorus Content µg./ml.	Sig.	Specific Activity	Corrected Specific Activity	Sig.
Intact	232 (13) *	88 ± 14 (25)		26.4 ± 7.2 (25)	58.5 ± 6.8 (13)	
Intact + DCA (Acute)	236 (11)	83 ± 15 (22)		25.9 ± 7.8 (22)	58.0 ± 7.6 (11)	
Intact	169 (10)	77 ± 12 (20)	S	33.1 ± 10.3 (20)	54.1 ± 12.1 (10)	S
Intact + DCA (Chronic)	191 (10)	89 ± 10 (20)	S	26.1 ± 11.6 (20)	48.6 ± 19.7 (10)	
Adrenalectomized	178 (12)	91 ± 20 (18)	S	45.9 ± 15.9 (18)	83.0 ± 29.6 (9)	
Adrenalectomized + DCA (Chronic)	192 (14)	89 ± 13 (24)		33.4 ± 9.1 (24)	64.2 ± 14.8 (12)	

* Figures in parenthesis indicate number of determinations

FIGURE V

PLASMA

EFFECT OF ADRENALECTOMY

EFFECT OF DCA

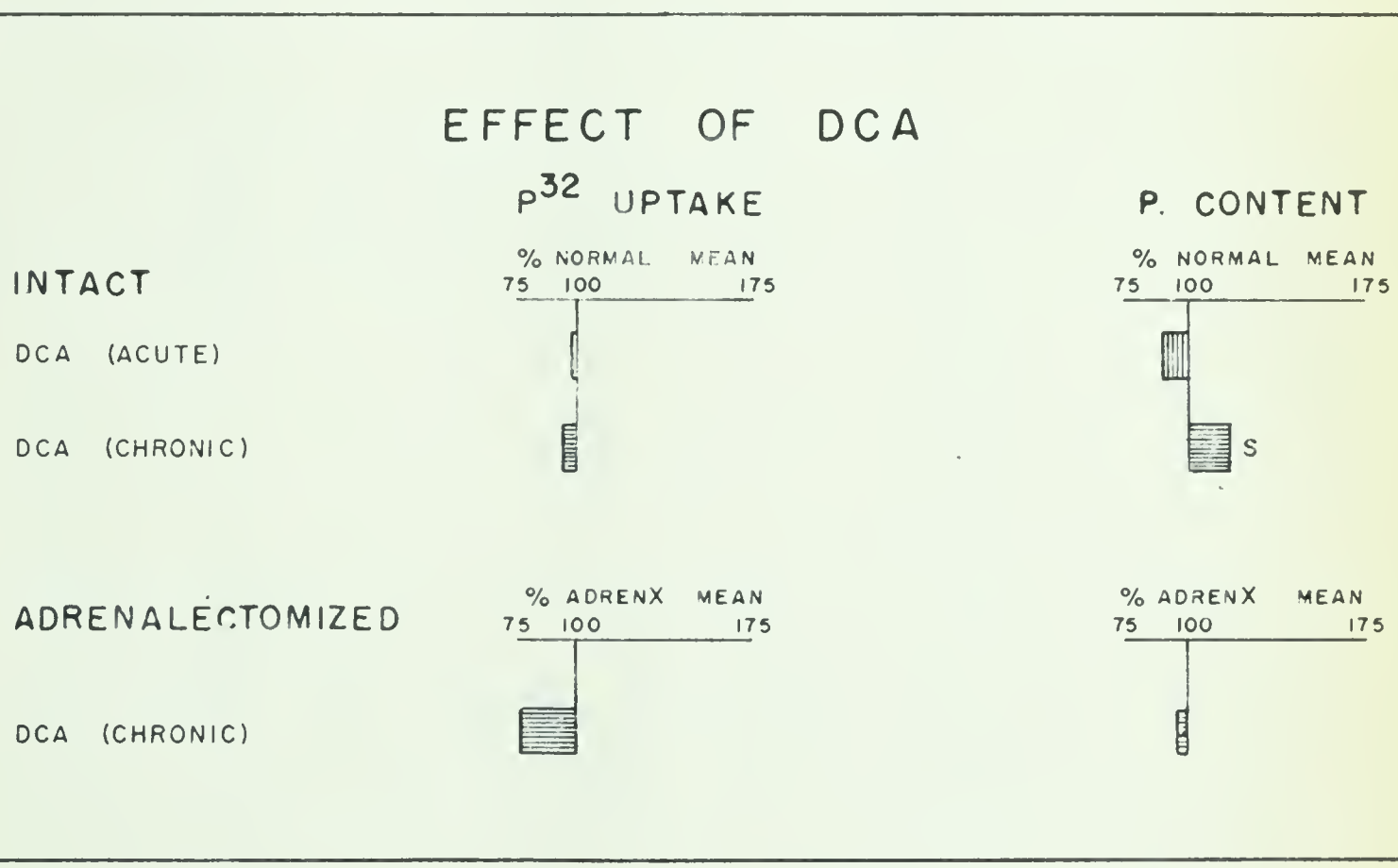


Table IX

ADRENAL - Effect of the Administration of DCA on QO_2, Phosphorus Concentration and P^{32} Incorporation

Group of Animals	QO_2 ml. O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Specific Activity	Relative Specific Activity	Sig.
Intact	2.57 ± 0.37 (11) *	S	1.24 ± 0.37 (24)	27.2 ± 9.2 (24)	462 ± 168 (24)	
Intact + DCA (Acute)	2.96 ± 0.26 (9)		1.17 ± 0.37 (20)	25.3 ± 5.7 (20)	429 ± 107 (20)	
Intact	2.62 ± 0.32 (9)		1.13 ± 0.24 (20)	25.2 ± 9.9 (20)	470 ± 171 (20)	
Intact + DCA (Chronic)	2.38 ± 0.15 (6)		1.14 ± 0.27 (10)	19.9 ± 10.0 (10)	378 ± 152 (10)	

* Figures in parenthesis indicate number of determinations

FIGURE VI

ADRENAL

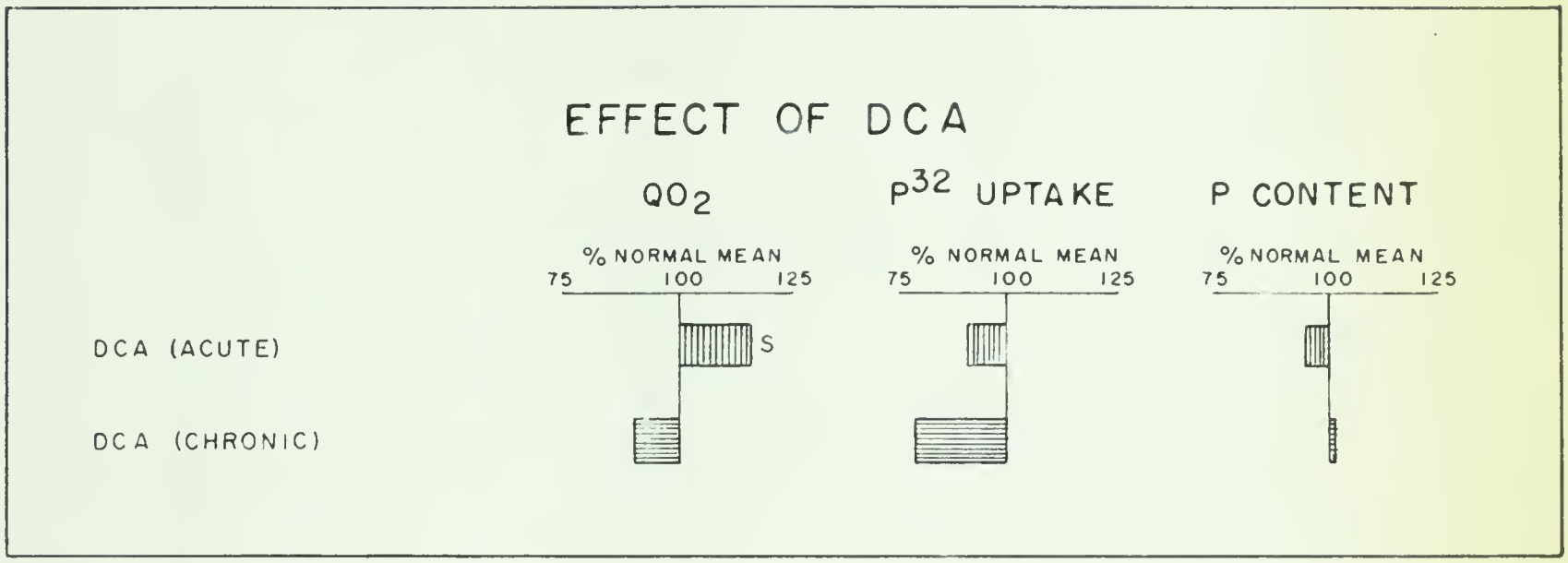


Table X

DORSOLATERAL PROSTATE - Effect of Adrenalectomy and the Administration of DCA on QO_2, Phosphorus Concentration and P^{32} Incorporation

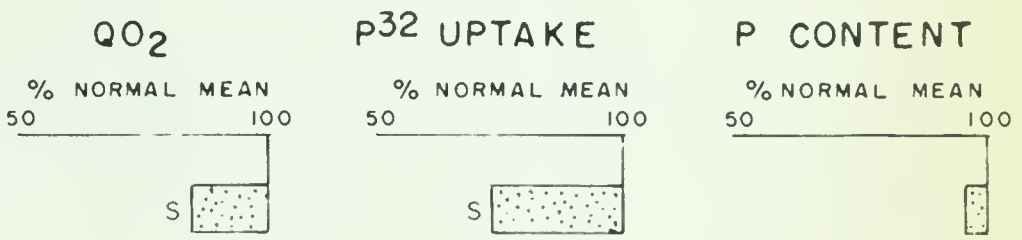
Group of Animals	QO_2 ml. O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Intact	0.91 ± 0.13 (11) *		1.99 ± 0.28 (26)		14.6 ± 3.1 (26)	253 ± 62 (26)	
Intact + DCA (Acute)	0.85 ± 0.12 (9)		1.86 ± 0.29 (22)		14.9 ± 4.4 (21)	256 ± 58 (21)	
Intact	0.95 ± 0.13 (9)	S	1.71 ± 0.32 (20)		17.8 ± 5.3 (20)	333 ± 90 (20)	S
Intact + DCA (Chronic)	0.76 ± 0.11 (11)	S	1.69 ± 0.31 (18)		17.8 ± 8.9 (18)	315 ± 114 (18)	S
Adrenalectomized	0.77 ± 0.13 (11)	S	1.66 ± 0.30 (20)		19.0 ± 3.9 (20)	247 ± 87 (18)	S
Adrenalectomized + DCA (Chronic)	0.75 ± 0.20 (14)	S	1.83 ± 0.67 (22)		17.8 ± 7.5 (22)	267 ± 91 (22)	S

* Figures in parenthesis indicate number of determinations

FIGURE VII

DORSOLATERAL PROSTATE

EFFECT OF ADRENALECTOMY



EFFECT OF DCA

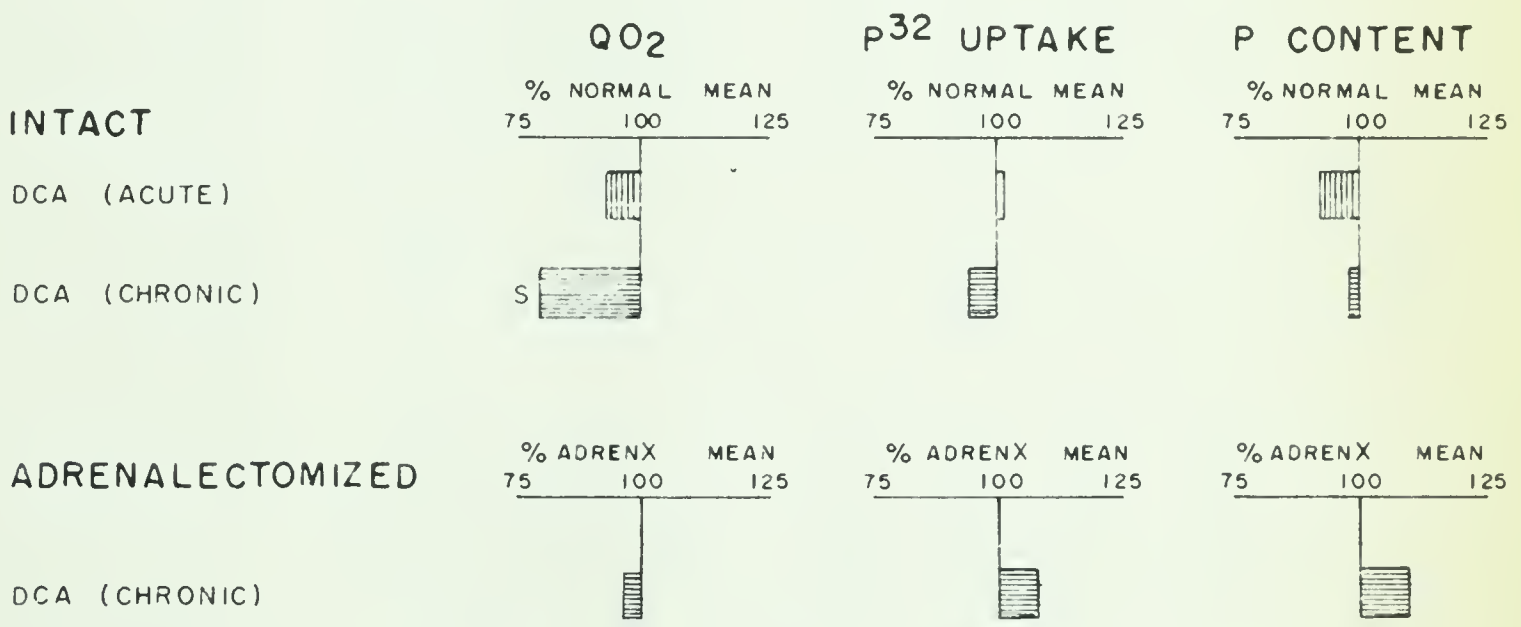


Table XI

VENTRAL PROSTATE - Effect of Adrenalectomy and the Administration of DCA on QO_2, Phosphorus Concentration and P^{32} Incorporation

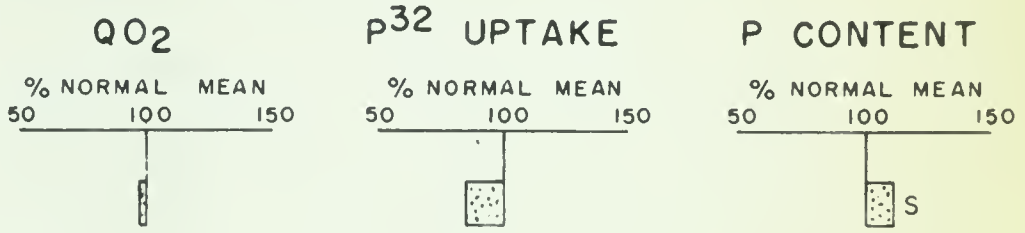
Group of Animals	QO_2 ml. O_2/Gm./hr.	Sig.	Phosphorus Content µg./mg.	Sig.	Specific Activity	Relative Specific Activity	Sig.
Intact	1.22 ± 0.13 (11) *		0.83 ± 0.17 (22)		23.9 ± 3.7 (22)	412 ± 53 (22)	
Intact + DCA (Acute	1.22 ± 0.11 (9)		0.76 ± 0.14 (22)		22.3 ± 3.2 (21)	391 ± 67 (21)	
Intact	1.12 ± 0.14 (8)		0.66 ± 0.06 (20)	S	25.1 ± 6.7 (20)	470 ± 116 (20)	
Intact + DCA (Chronic)	1.19 ± 0.19 (11)		0.88 ± 0.17 (18)		24.9 ± 11.6 (18)	443 ± 121 (18)	
Adrenalectomized	1.10 ± 0.20 (12)		0.74 ± 0.15 (20)	S	30.5 ± 4.4 (20)	401 ± 122 (18)	
Adrenalectomized + DCA (Chronic)	1.04 ± 0.18 (13)		0.69 ± 0.11 (24)		30.1 ± 7.7 (24)	469 ± 80 (24)	

* Figures in parenthesis indicate number of determinations

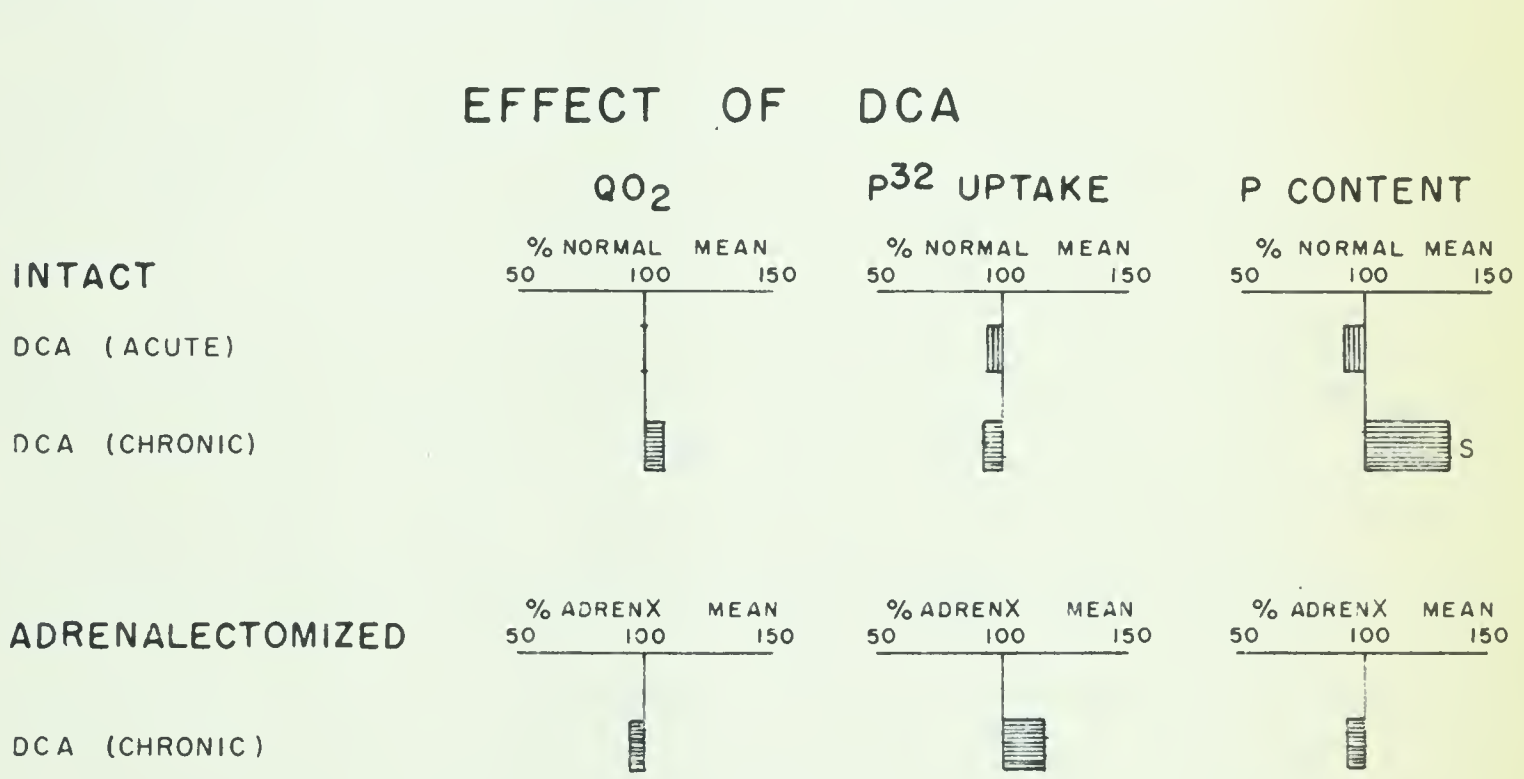
FIGURE VIII

VENTRAL PROSTATE

EFFECT OF ADRENALECTOMY



EFFECT OF DCA



V DISCUSSION

A. GENERAL DISCUSSION

A discussion of the results of tissue respiration should be prefaced by some comments on the procedure proposed by Huston and Martin for the determination of tissue respiration in contact with oxygen. In standard Warburg methods the tissues are suspended in solutions approximating the milieu intérieur. The suspending media dilute and may modify cellular metabolites, hormones and other substances found in the cells of living tissues. Also, the added materials may influence the normal rate of respiration. Cellular effects demonstrated by the addition of drugs *in vitro* do not necessarily represent the response of the intact animal, particularly in view of possible differential tissue distribution and sensitivity of the drug. The interpretation of pharmacological investigations are complicated by these physiological uncertainties. Huston and Martin (94) described a method for the determination of the respiratory rates of tissues in contact with oxygen by supporting them in the gas phase on fiber glass mats in a modified wide-mouthed Warburg flask. Using this technique the respiratory rates of tissues can be measured without the introduction of the uncertainties of an artifical liquid medium.

Some limitations of this technique are:

(a) once the tissue is placed on the mat, further drugs and metabolites cannot be added. The technique therefore does not lend itself to an examination of substrate phenomena;

(b) the tissue cannot act as its own control as is the case when the drug is added from a side arm. It is therefore necessary to run control series of non-treated animals;

(c) a disadvantage, and one which is inherent in all tissue respiration studies, is that once the tissue is removed from the body it progressively departs from physiological normalcy. Many factors are involved, not all of which are known. Some of the more obvious factors are loss of hormone and nervous control, limitation of supply of metabolites and ions and accumulation of metabolic end products. However, since the primary interest is the effect of the drug on the tissue at the time it is removed from the body, that is the in vivo effect, this disadvantage is not serious.

(d) a possible disadvantage is that the tissue is in contact with oxygen and not supplied with nutrient and thus may consume all its endogenous substrates. This situation would be indicated by a more rapid fall in the slope of the graph and at the end of an hour the respiration rate might be expected to be below that of the tissues in fluid.

However, it was found that the tissues on the mats had the least diminution of oxygen consumption (94).

The above disadvantages are minimized by the procedure of extrapolation to zero time. The rate of respiration has been reduced in the cold during the preliminary manipulations and returns to a maximum at the conclusion of equilibration which is the point of extrapolation. This figure would appear to closely approximate the in vivo situation.

Stare and Elvehjem (102) postulated that the oxygen uptake of each tissue is a measure of the sum total of the activity of the various individual oxidase systems. A deviation from the normal respiration of the tissue could therefore be due to pathological changes in the activity of the individual enzyme systems. Huston and Martin felt that results obtained by using their method were reliable approximations to in vivo conditions.

The interpretation of changes in phosphorus metabolism should also be commented upon. The adrenal ascorbic acid depletion test of Sayers (103) is the most widely used method for the assay of ACTH. Nicholls and Graham (78) suggested that the incorporation of inorganic P^{32} into the adrenal gland could also be used as an index of the stimulation of the adrenal cortex by ACTH, since substances which are known to cause depletion of adrenal ascorbic acid, increased the relative specific activity of the adrenal gland. Thus either the administration of ACTH to hypophysectomized rats or the exposure of normal rats to a cold environment caused an increase in the rate at which inorganic phosphate labelled with radioactive phosphorus (P^{32}) entered the cellular portion of the gland (59, 60, 64, 69, 76). Administration of ACTH to

hypophysectomized rats (103) or exposure of normal rats to a cold environment (104) caused a depletion of adrenal ascorbic acid. The evidence for the assumption, (that increased incorporation of inorganic P^{32} into the adrenal gland is indicative of stimulation of the adrenal cortex by ACTH), is indirect, but, is of the same type as that favoring the view that the depletion of adrenal ascorbic acid is a measure of adrenal cortex stimulation (78).

B. DISCUSSION OF RESULTS

1. Effect of Hypophysectomy and the Administration of ACTH

The effects of hypophysectomy and the administration of ACTH are discussed for the individual tissues.

a. Plasma

The normal mean value obtained for the inorganic phosphorus concentration in rat plasma was found to vary from series to series. The average mean plasma phosphorus concentration observed in this investigation was 90 µg. P/ml. plasma (9.0 mg./100 ml.). This value is within the range reported by others. Gemzell and Samuels (59) reported a figure of 5.36 mg./100 ml. and Li et al (61) found that the concentration of plasma inorganic phosphorus was 11.4 mg./100 ml. Variations in the extraction methods and quantitative determinations might contribute to these differences.

The mean value observed for plasma phosphorus concentration in rats sacrificed at intervals 4 to 20 days after hypophysectomy was significantly less than normal. This effect of hypophysectomy has been previously reported (59-61). A slight decrease was found in plasma phosphorus concentration 4 days after

hypophysectomy but this reduction was not significant. In contrast, Li et al (61) and Riedel et al (60) found that in hypophysectomized rats, the plasma phosphorus concentration was reduced 2 days postoperative and gradually fell over a 14 day period.

Gemzell and Samuels (59) suggested that either increased excretion or increased storage in bone could account for the decreased concentration of plasma inorganic phosphorus observed in hypophysectomized animals. Geschwind et al (63), however, reported a decreased total amount of phosphorus per unit weight of bone in hypophysectomized rats. They suggested that lack of growth hormone in hypophysectomized animals might account for the decreased plasma phosphorus concentration since Li et al (61) had previously reported that when growth hormone was administered to hypophysectomized animals, the plasma concentration of phosphorus did not fall but was elevated above that of normal controls.

Gemzell and Samuels (59) reported that ACTH caused a further significant decrease in plasma inorganic phosphorus concentration in hypophysectomized animals. However in this study, an intraperitoneal injection of ACTH did not significantly alter the plasma phosphorus level in either normal or hypophysectomized rats. Other workers have reported that ACTH had no effect on plasma phosphorus concentration (60,66).

The plasma corrected specific activity in the 4 - 20 day hypophysectomized rats was significantly higher than normal. This observation is in agreement with the results of other workers (59, 60, 63 - 65). A similar increase in plasma corrected specific

activity was found 4 days after hypophysectomy but this elevated level of P^{32} was not significantly different from the normal level. Riedel et al (65) and Logan et al (66) found no significant change in the specific activity of plasma phosphorus 16 hours after injection of P^{32} in 2 day hypophysectomized rats. However, at shorter time intervals after P^{32} injections, 50 minutes (59) and 2 hours (60), there was an increase in the specific activity of plasma phosphorus, 5 days and 2 days after hypophysectomy, respectively.

Gemzell and Samuels (59) suggested that there might be a reduced rate of exchange of inorganic phosphorus between the extracellular and intracellular compartments. Geschwind et al (63) showed that in hypophysectomized animals there was a decreased uptake of P^{32} by muscle and bone. This effect of hypophysectomy would tend to elevate the activity in plasma. In addition, Geschwind and co-workers suggested that the smaller mass per unit body weight of some soft tissues (eg., liver) would result in a decreased total P^{32} uptake by these organs. These workers also suggested that a predicted decrease in the uptake of P^{32} by target organs affected by hypophysectomy would elevate the plasma P^{32} level. These workers showed that growth hormone was capable of lowering the plasma P^{32} level in hypophysectomized animals toward normal. Lack of growth hormone in hypophysectomized animals would seem to be responsible, in part at least, for the abnormal plasma inorganic phosphorus concentration and specific activity.

ACTH has been shown in these experiments and by others (59, 65) to have little effect upon plasma phosphorus concentration or specific activity in hypophysectomized or normal animals.

Since a part of the present study was designed to investigate the uptake of P^{32} by the adrenal and prostate from the plasma, the cause of the increased plasma specific activity in hypophysectomized animals was not investigated further. An increased rate of absorption of P^{32} from the peritoneal cavity or a decreased elimination of P^{32} by the kidney of hypophysectomized animals are other possibilities that could be explored. The decrease in the concentration of the inorganic phosphorus of the plasma discussed above is not large enough to explain the increase in the specific activity.

b. Adrenal

The marked effects observed of hypophysectomy and ACTH on QO_2 and P^{32} uptake are indicative of the control that the hypophysis has on the adrenal gland.

The mean adrenal QO_2 of rats sacrificed at intervals from 4 to 20 days after hypophysectomy was less than one-half of the normal QO_2. The mean adrenal QO_2 4 days postoperative was reduced by one-quarter. However, insufficient data was available for different time intervals after hypophysectomy to show statistically that the mean adrenal QO_2 diminished with time after hypophysectomy. The percentage increase in adrenal QO_2 in response to ACTH was approximately the same in normal and hypophysectomized animals. These observations would indicate that exogenous ACTH is able to stimulate the adrenal QO_2 in the presence or absence of the hypophysis, and, also, that in the absence of endogenous ACTH, the QO_2 is reduced. *In vivo* administration of ACTH to intact rats has been previously reported to increase the adrenal QO_2 (79).

Overbeek and Van der Vies (82) suggested that the percentage increase in QO_2 consumption in response to in vitro addition of ACTH to homogenized hog adrenal cortex could be employed in a biological assay of ACTH.

It has been shown that O^{18} enters the 11-beta position in steroid hydroxzlations from molecular O^{18} but not from H_2O^{18} (15). Since it has been shown conclusively that ACTH stimulates corticoidogenesis (28), the increased adrenal QO_2 after ACTH treatment observed in this study, could be indicative of stimulated corticoidogenesis.

The adrenal concentration of phosphorus was increased in both hypophysectomized groups. This effect of hypophysectomy has been previously reported (59). Gemzell and Samuels (59) suggested that the increased concentration of inorganic phosphorus in the adrenal after hypophysectomy may be due to decreased incorporation of the phosphorus into esters and phospholipids.

Administration of ACTH did not significantly affect the adrenal phosphorus concentration in either normal or hypophysectomized rats. Other workers have reported that the adrenal acid soluble phosphorus concentration was unchanged after hypophysectomy (60,64) or ACTH treatment of either normal or hypophysectomized rats (64).

In this investigation it was found that the relative specific activity of the adrenal acid soluble fraction was reduced by approximately one-quarter in both hypophysectomized series. This observation that hypophysectomy reduced the adrenal incorporation of P^{32} is in agreement with previous reports (59, 60, 63, 64, 66).

The reduction in P^{32} incorporation in the adrenal 4 to 20 days after hypophysectomy was not as great as the reduction in the adrenal QO_2 in the same series. This observation might indicate that different mechanisms influence the P^{32} uptake in the acid soluble fraction of the adrenal and the adrenal QO_2.

The percentage increase in adrenal relative specific activity (24 hours after a single injection of ACTH) was approximately the same in both normal and hypophysectomized rats. Other investigators have reported that administration of ACTH increased the specific activity in both normal rats (66, 69) and hypophysectomized rats (59, 60, 66, 69).

The percentage increase in adrenal relative specific activity after ACTH treatment was considerably greater than the percentage increase in adrenal QO_2. This observation lends further support to the suggestion that the incorporation of P^{32} and QO_2 of the adrenal are influenced by different mechanisms.

Since exogenous ACTH stimulated the incorporation of P^{32} into the acid soluble fraction of the adrenal in both normal and hypophysectomized animals, and, since the removal of the endogenous source of ACTH reduced the P^{32} uptake, it would appear that ACTH influences the adrenal incorporation of P^{32}, as well as the adrenal QO_2.

Logan, Riedel, and Rossiter (73) postulated that ACTH increases the permeability of P^{32} into the adrenal cell. In this investigation, it was found that ACTH did not affect the concentration of acid - soluble phosphorus. The increased level of activity found in the adrenal after ACTH treatment could therefore

be due to a true increase in the turnover of acid soluble phosphorus compounds, as well as an increased transfer of inorganic phosphorus across the adrenal cell membranes.

In addition to the decrease in the relative specific activity of the inorganic phosphorus in the adrenal gland of hypophysectomized rats, Riedel, Logan and Rossiter (65) found a decrease in the concentration and in the specific activity of adrenal lipid phosphorus. These workers suggested that the decreased incorporation of P^{32} into lipid phosphorus might be secondary to the reduction in the rate at which inorganic phosphorus passes through the adrenal cell membrane. They also suggested that there may be a decreased formation of phospholipids from the intracellular inorganic phosphorus. These investigators postulated the possibility that these changes in lipid phosphorus metabolism could reflect a marked decrease in the total energy metabolism of the adrenal cell.

Further support was given by Logan, Heagy and Rossiter (66) for the thesis that hypophysectomy caused a marked decrease in the total energy metabolism of the adrenal cell. These workers found that hypophysectomy reduced the concentration and incorporation of P^{32} into adrenal nucleotides. A single injection of ACTH reversed these effects of hypophysectomy.

From recent research, reviewed by Saffran (28) a scheme has been proposed in which ACTH stimulates the accumulation of 3', 5' AMP within the adrenal cell. 3', 5' AMP, by stimulating phosphorylase activity, subsequently increases the amount of adrenal TPNH. TPNH has been reported necessary in the formation of corticoids (15). Although the experimental conditions differ, this observation that ACTH ultimately stimulates the phosphorylase activity in the adrenal cell, would suggest that the increased P^{32}

activity in the adrenal (in response to ACTH) is the result of an increased rate of turnover of acid soluble phosphorylated compounds.

c. Dorsolateral Prostate and Ventral Prostate

Although four day hypophysectomy did not appear to affect either dorsolateral prostate or ventral prostate QO_2, longer term hypophysectomy (four to twenty days) reduced the QO_2 in both prostate portions. The percentage decreases in the mean QO_2 of the two prostate portions four to twenty days after hypophysectomy were approximately equal, but were not as great as the percentage decrease in adrenal QO_2 in the same series. This observation would suggest that the prostate QO_2, as well as the adrenal QO_2, is influenced by the hypophysis. In addition to the observation that the magnitude in reduction of QO_2 was greater in the adrenal than in the prostate, the fact that the adrenal QO_2 was reduced four days postoperative and the prostate QO_2 was unchanged at this time, would suggest that the hypophysis has greater influence on the QO_2 of target organs than on the QO_2 of other parts of the rat body.

Four days after hypophysectomy was sufficient time to observe a change in concentration of acid soluble phosphorus in the prostate. The dorsolateral prostate phosphorus concentration was reduced, whereas, the ventral prostate phosphorus concentration was increased. It has been reported that hypophysectomized animals lose more water and protein and much less fat than normal rats (105). Such a loss in water and protein and consequent loss in tissue weight might not be accompanied by a loss in phosphorus.

This could explain why the phosphorus concentration, which is based on the wet weight of the tissue was increased in the ventral prostate. It would not, however, explain the decreased phosphorus concentration in the dorsolateral prostate, which could therefore be due to a true reduction in the phosphorus concentration.

Similar to the effect of hypophysectomy upon prostate QO_2, the specific activity of either dorsolateral or ventral prostate acid soluble phosphorus was unaltered four days after hypophysectomy. A significant increase in specific activity and relative specific activity of both prostate portions was observed four to twenty days following hypophysectomy. It is tempting to attribute the increased level of P^{32} in the prostate in the longer term hypophysectomized rats to the increased level of P^{32} in the plasma. Geschwind and his co-workers (63) were of the opinion that the high P^{32} activities in soft tissues (liver, kidney, thymus) of hypophysectomized animals simply reflected the high plasma activities.

ACTH did not significantly affect the QO_2, phosphorus concentration or incorporation of P^{32} in either of the prostate portions in hypophysectomized animals. In normal rats (Series IV) ACTH, significantly increased ventral prostate phosphorus concentration but decreased the specific activity and relative specific activity. However, in the other experiments (Series II-IV) the administration of ACTH did not significantly affect any measurements performed on the rat prostate.

2. Effects of Adrenalectomy and the Administration of DCA

(a) Plasma

The results reported here and by others (106) have shown that adrenalectomy increases the plasma concentration of inorganic phosphorus. In this investigation, adrenalectomy also increased the plasma specific activity. The decreased plasma volume in adrenalectomized animals (12) with subsequent concentration in plasma constituents may contribute to the explanation of these observations.

Since chronic administration of DCA depressed the plasma specific activity in both intact and adrenalectomized animals, the mineralocorticoid may have a direct action on the removal of P^{32} from the plasma. Mills and Thomas (107) suggested that corticoids caused a fall in plasma phosphorus concentration by increasing the permeability of cell membranes to phosphate and by stimulating some active process in phosphorus uptake. They further suggested that, since glucocorticoids increase the liver glycogen, the disappearance of phosphate from the plasma may be associated with the deposition of glycogen. Although slight in comparison with the glucocorticoids, hydrocortisone and cortisone, DCA does increase liver glycogen (50).

As previously mentioned, this investigation was not designed to study the effects of hypophysectomy or adrenalectomy on the plasma specific activity. It is interesting, however, that in both cases, the plasma specific activity was increased. Further work could be done in an attempt to elucidate the hormonal control of the plasma level of P^{32}.

(b) Adrenal

Chronic administration of DCA reduced both the QO_2 and the relative specific activity of the adrenal. However, these decreases were not significant. Others reported that prolonged cortisone treatment reduced the adrenal respiration (93) and incorporation of P^{32} (75).

(c) Dorsolateral Prostate and Ventral Prostate

Part B of this study was conducted primarily to observe the effects of adrenalectomy and the administration of DCA on the tissue respiration and phosphorus metabolism of the prostate. Rudzik and Riedel (4) reported that adrenalectomy reduced the zinc concentration and incorporation of Zn^{65} in the dorsolateral prostate. They suggested that the dorsolateral prostate is dependent upon normal adrenal activity for proper functional activity. In this investigation it was found that adrenalectomy or suppression of adrenal activity with DCA reduced the dorsolateral prostate QO_2. Adrenalectomy also reduced the relative specific activity of this gland.

Unlike the dorsolateral prostate, the ventral prostate QO_2 and relative specific activity were unaltered by adrenalectomy or chronic administration of DCA. Rudzik and Riedel suggested that these two lobes of the prostate were functionally different organs since adrenalectomy did not alter the ventral prostate zinc concentration or Zn^{65} incorporation.

Although the experimental conditions differ, from the effects of adrenalectomy on prostate QO_2 and P^{32} uptake observed

in this investigation and from the effects of adrenalectomy on zinc metabolism of the prostate observed by Rudzik and Riedel , two suggestions can be made:

1. The dorsolateral prostate QO_2, P^{32} incorporation and zinc metabolism are dependent upon normal adrenal activity, and
2. The two lobes of the prostate are functionally different.

VI SUMMARY

The aim of this research was to determine the effects of altered adrenal states on the tissue respiration and phosphorus metabolism in the adrenal gland and the dorsolateral prostate and ventral prostate glands.

1. It was found that hypophysectomy significantly depressed the respiration of adrenal and prostate tissues.
2. Hypophysectomy reduced the relative specific activity of the adrenal. In contrast, an increased level of P^{32} was found in the prostate and plasma.
3. Administration of ACTH significantly increased both the tissue respiration and the incorporation of P^{32} in the adrenal of normal animals and hypophysectomized rats.
4. A single injection of ACTH had little effect on prostate respiration or on prostate or plasma phosphorus metabolism, in either normal or hypophysectomized animals.
5. A single injection of DCA increased adrenal QO_2. No other effects were observed in adrenal, prostate or plasma metabolism.
6. Daily injections of DCA in normal rats reduced adrenal and dorsolateral prostate QO_2 and adrenal relative specific activity. Adrenalectomy reduced dorsolateral prostate QO_2 and relative specific activity.
7. The ventral prostate QO_2 and relative specific activity were unaltered by either chronic administration of DCA or adrenalectomy.
8. Adrenalectomy increased the plasma specific activity. Chronic DCA treatment reduced the plasma specific activity

in both normal and adrenalectomized rats.

9. The significance of the findings is discussed.

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A P P E N D I X

Table I

P L A S M A

Effect of the Administration of ACTH on Phosphorus Concentration and P^{32} Incorporation

Intact Guinea Pigs

Non-treated

Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity
500	-	-	-
504	-	-	-
948	64	-	-
	62	-	
	59	-	
	64	-	
840	69	83	128.4
	37	153	
	40	146	
	36	160	
620	134	69	38.9
	115	56	
	86	70	
	126	56	
568	88	99	53.9
	124	83	
	81	103	
598	79	58	35.5
	77	61	
	72	60	
	107	41	
772	77	58	50.1
	114	37	
	65	66	
	63	69	
612	107	60	36.7
	108	60	
	98	63	
	106	56	
N 9	27	23	6
Mean 662	84	77	57.3
S.D.	25	33	32.6

ACTH-treated

Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity
562	60	-	-
	64	-	
832	88	-	-
	89	-	
	90	-	
	90	-	
788	52	-	-
	56	-	
	53	-	
	58	-	
815	132	29	31.1
	128	29	
	79	53	
	87	41	
770	122	22	17.5
	105	23	
667	113	43	29.9
	131	40	
	106	48	
	111	48	
754	132	39	32.2
	115	44	
	116	43	
	111	45	
752	73	55	37.5
	90	44	
684	111	49	32.6
	121	45	
	109	49	
	109	48	
N 9	30	20	6
Mean 736	97	42	30.1
S.D.	25	9	7.4

Intact Rats

Non-treated

Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity
293	-	-	-
221	-	-	-
261	-	-	-
284	-	-	-
315	-	-	-
273	-	-	-
259	-	-	-
288	-	-	-
257	93	25.8	56.8
	120	18.4	
201	89	34.8	59.5
	125	24.3	
283	152	34.6	94.1
	144	32.0	
238	150	35.8	83.5
	154	34.4	
259	93	23.8	69.1
	90	29.6	
292	133	16.6	48.5
	118	16.6	
260	86	25.3	52.3
	128	15.0	
N 15	14	14	7
Mean 266	120	26.2	66.3
S.D.	25	7.2	15.7

ACTH-treated

Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity
284	-	-	-
209	-	-	-
327	206	33.0	79.7
	220	34.6	
273	105	34.6	94.4
	109	34.6	
249	99	34.5	80.4
	114	31.1	
249	105	21.3	51.8
	118	20.2	
314	100	20.8	64.1
	108	20.0	
290	112	22.5	59.5
	98	18.4	
N 8	12	12	6
Mean 263	125	27.3	71.7
S.D.	40	6.7	14.1

Table II

P L A S M A

Effect of Hypophysectomy and the Administration of ACTH on Phosphorus Concentration and P^{32} Incorporation

Intact				Hypophysectomized (4 - 20 days)							
Non-treated				Non-treated				ACTH-treated			
Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity	Animal Weight (gm.)	P µg./ml	Specific Activity	Corrected Specific Activity	Animal Weight (gm.)	P µg./ml	Specific Activity	Corrected Specific Activity
177	72	33.0	55.4	139	59	51 9	73 3	150	72	35 2	55 6
	77	31.6			59	53 4			71	38 8	
205	83	20 5	41 8	136	72	40 3	57 5	144	61	45 5	63 8
	81	20.4			68	44 3			60	43 0	
227	74	21.3	48.6	151	83	32 6	49 8	149	136	48 8	72 6
	75	21.4			87	33 4			140	48 6	
271	75	21.5	57.2	153	95	42 9	65 8	144	68	42 9	61 5
	72	20.8			93	43.1			71	42 5	
274	75	21.5	51.0	147	51	54 0	75 7	139	60	90 3	115 8
	88	15.6			58	48 9			65	76 2	
292	73	26.5	70 7	157	61	42 1	63 9	142	79	55 1	76 3
	68	21.9			60	39 3			78	52 3	
288	77	17.0	54.4	135	81	53 7	77 2	136	67	50 2	68 7
	79	20.8			80	60.7			67	50 7	
299	84	14.3	45.6	128	82	62 7	79 0	135	72	57 8	74 9
	75	15.6			81	60 7			73	53 1	
166	-	-	-	130	46	56 5	74 5	150	66	57 7	86 3
172	73	32 4	56.1		46	58 1			69	57 3	
	73	32 7		152	55	54 0	80 3	150	50	50 2	79 1
180	92	27.9	49.1		55	51 6			47	55 1	
	94	26.6		145	63	57 5	80 6	147	72	59 8	84 1
					58	53 7			70	54 5	
				137	70	54 9	74 0	135	79	54 5	75 3
					69	53 2			78	57 0	
				140	63	57 7	82 0				
					63	59 4					
N 11	20	20	10	N 13	26	26	13	N 12	24	24	12
Mean 232	78	23.2	53 0	Mean 142	68	50 8	71 8	Mean 143	74	53 2	76 2
S.D.	6	5.7	7.5	S.D.	14	8 3	9.4	S.D.	21	11 2	14 7

Table III

R A T P L A S M A

Effect of Hypophysectomy and the Administration of ACTH on Phosphorus Concentration and P^{32} Incorporation

Intact								Hypophysectomized (4 days)							
Non-treated				ACTH-treated				Non-treated				ACTH-treated			
Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity	Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity	Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity	Animal Weight (gm.)	P µg./ml.	Specific Activity	Corrected Specific Activity
156	90	34.2	54.0	153	84	29.2	46.4	141	-	-	-	147	64	43.7	63.7
	82	35.0			82	31.3		145	84	49.3	68.4		60	42.8	
187	79	30.4	55.9	189	82	34.4	63.5		79	45.0		148	81	36.0	52.7
	93	29.4			82	32.7		143	98	34.9	49.5		88	35.2	
173	92	27.7	44.6	172	83	24.7	42.8		98	34.2		138	93	35.4	49.1
	100	23.9			83	25.0		156	89	37.3	58.8		96	35.7	
173	78	34.6	62.1	172	78	34.6	58.8		87	38.1		169	86	32.8	60.0
	79	37.2			92	33.8		145	83	28.3	40.0		84	38.2	
163	82	32.5	51.7	158	-	-	-		89	26.8		143	96	33.5	49.8
	85	30.8		163	88	29.3	50.0	155	97	38.2	59.1		96	36.0	
165	94	31.8	52.8		90	32.0			105	37.9		153	114	38.0	62.3
	92	32.2						132	71	44.2	60.3		106	43.4	
									72	47.2		139	67	45.3	61.7
								157	63	34.5	55.4		78	43.4	
									75	36.1		153	97	33.4	50.0
													99	31.9	
N 6	12	12	6	N 6	10	10	5	N 8	14	14	7	N 8	16	16	8
Mean 170	87	31.6	53.5	Mean 168	84	30.7	52.3	Mean 147	85	38.0	55.9	Mean 149	88	37.8	56.2
S.D.	7	3.4	5.2	S.D.	4	3.4	7.7	S.D.	12	6.3	8.4	S.D.	15	4.3	5.9

Table IV

A D R E N A L

Effect of the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact Guinea Pigs

Non-treated

QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
1.75	-	-	-
1.54	-	-	-
1.80	-	-	-
1.50	-	-	-
1.78	-	-	-
1.84	-	-	-
1.75	-	-	-
1.53	-	-	-
1.83	1.24	-	-
1.68	1.28	-	-
1.72	1.21	-	-
1.53	1.19	-	-
1.64	1.47	44.5	346
1.68	1.44	44.2	344
1.75	1.66	42.4	330
1.22	1.60	43.4	338
2.15	-	-	-
1.90	-	-	-
1.82	1.43	48.2	1240
1.92	1.45	63.6	1637
1.82	1.32	67.1	1245
1.77	1.38	67.4	1251
-	1.38	63.1	1171
1.73	1.37	65.7	1219
-	1.34	19.5	549
1.63	1.33	18.6	524
1.87	1.47	20.9	589
1.78	1.33	21.6	608
1.77	1.49	52.9	1056
1.53	1.38	56.2	1122
1.65	1.39	54.3	1084
1.80	1.38	55.7	1112
2.32	2.74*	39.2*	1068*
1.87	2.56*	41.4*	1128*
2.30	2.16*	41.5*	1131*
1.84	2.30*	40.1*	1093*
N 34	22	18	18
Mean 1.77	1.39	47.2	876
S.D. 0.21	0.11	16.5	598

* Omitted from statistical analysis

ACTH-treated

QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
1.08*	1.74	-	-
1.27*	1.94	-	-
1.40*	1.65	-	-
1.24*	1.54	-	-
1.87	1.47	-	-
2.10	1.48	-	-
1.87	1.49	-	-
1.71	1.56	-	-
2.05	1.20	-	-
1.70	1.39	-	-
2.12	1.42	-	-
1.76	1.54	-	-
1.45*	1.86	45.8	1473
1.50*	1.71	50.1	1611
1.43*	1.85	42.4	1363
1.73*	1.67	44.4	1428
1.45*	1.44	37.5	2143
1.35*	1.57	35.4	2023
1.35*	1.52	38.4	2194
1.50*	1.55	37.1	2120
1.98	-	-	-
1.70	-	-	-
2.12	1.63	44.1	1475
2.23	1.62	43.5	1455
2.03	1.85	40.3	1251
2.15	1.82	40.5	1256
1.85	1.89	28.7	891
1.90	1.35	38.7	1200
2.12	2.62*	25.5*	682*
2.10	1.54	46.7	1247
2.00	2.78*	23.5*	627*
1.90	2.67*	27.2*	727*
2.18	1.49	36.1	1107
2.20	1.71	33.0	1012
2.32	1.60	36.2	1111
1.98	1.62	35.6	1091
N 24	31	19	19
Mean 2.00	1.60	39.7	1445
S.D. 0.20	0.17	5.1	389

* Omitted from statistical analysis

Intact Rats

Non-treated

QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
2.36	-	-	-
2.09	-	-	-
1.75	-	-	-
1.97	-	-	-
1.62	-	-	-
2.10	-	-	-
2.23	-	-	-
2.30	-	-	-
3.15	1.54	17.6	320
	1.48	17.4	306
2.45	2.78	12.4	208
	1.76	17.3	291
2.20	1.21	25.1	268
	1.22	26.3	280
2.93	1.54	24.5	293
	1.47	22.3	267
2.07	0.93	20.8	301
	0.93	23.1	334
2.28	1.17	23.8	491
	1.26	21.2	437
1.70	1.05	28.6	547
	1.45	17.5	335
N 15	14	14	14
Mean 2.21	1.41	21.3	334
S.D. 0.40	0.45	4.2	90

ACTH-treated

QO_2 ml. O_2/gm./hr	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
2.70	-	-	-
2.92	1.70	34.7	-
	1.44	36.7	-
2.85	1.44	34.4	432
	1.35	32.9	413
3.00	1.35	34.9	370
	1.52	32.8	347
2.83	1.64	39.4	490
	1.69	37.8	470
2.65	1.15	47.2	911
	1.17	27.7	535
2.90	1.19	23.8	371
	1.23	32.0	499
3.30	1.25	30.0	504
	1.15	32.1	539
N 8	14	14	12
Mean 2.89	1.38	34.0	490
S.D. 0.19	0.67	5.3	142

Table V

R A T A D R E N A L

Effect of Hypophysectomy and the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact

Non-treated

QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
2.65	1.80	15.0	271
	1.85	15.9	287
3.07	1.82	16.8	402
	1.81	16.4	392
2.34	1.22	18.3	377
	1.23	18.0	370
2.52	1.27	20.2	353
	1.34	21.2	370
3.23	1.24	20.4	400
	1.31	19.4	380
2.88	1.25	35.9	508
	1.24	26.6	376
2.87	1.09	13.8	254
	1.07	12.6	232
2.88	1.19	5.6	123
	1.35	10.1	221
2.75	-	-	-
2.93	1.18	22.2	396
	1.19	23.8	424
2.78	1.41	28.4	578
	1.34	27.6	562
N 11	20	20	20
Mean 2.81	1.36	19.4	364
S.D. 0.23	0.24	6.7	109

Hypophysectomized (4 - 20 days)

Non-treated

QO_2 ml. O_2/gm./hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
1.11	0.96	31.7	432
	1.03	27.2	371
1.34	1.76	15.4	268
	1.60	18.1	315
1.04	2.19	10.1	203
	2.16	9.0	181
0.93	2.03	12.1	184
	2.10	12.7	193
1.13	2.19	10.5	139
	2.06	11.0	145
1.15	1.79	11.9	186
	1.72	11.9	186
1.06	1.83	24.4	316
	1.85	24.1	312
0.95	1.83	28.4	359
	1.70	27.6	349
1.18	1.15	37.9	509
	1.18	39.3	528
1.62	2.32	12.0	149
	2.39	13.4	167
1.25	1.67	19.8	247
	1.64	19.0	236
0.82	1.25	22.0	297
	1.32	22.1	299
1.09	1.30	28.1	343
	1.28	26.3	321
N 13	26	26	26
Mean 1.13	1.70	20.2	278
S.D. 0.19	0.41	8.6	105

ACTH-treated

QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
2.31	1.13	46.8	842
	1.20	42.2	759
1.72	1.26	39.8	624
	1.23	34.1	534
1.22	-	-	-
1.48	2.48	18.9	307
	2.48	19.4	315
1.25	-	-	-
0.93	1.83	42.5	557
	1.91	40.9	536
1.20	1.93	25.1	365
	1.87	25.0	364
1.20	1.61	41.9	559
	1.57	45.1	602
1.47	2.62	25.4	294
	2.70	26.1	302
0.96	2.67	22.2	281
	2.35	25.0	316
1.43	1.06	55.4	659
	1.03	60.0	713
1.15	1.32	54.1	718
	1.38	54.8	728
N 12	20	20	20
Mean 1.36	1.78	37.2	519
S.D. 0.36	0.57	12.8	181

Table VI

R A T A D R E N A L

Effect of Hypophysectomy and the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

	Intact				Hypophysectomized (4 days)			
	Non-treated		ACTH-treated		Non-treated		ACTH-treated	
	QO_2 ml. O_2/gm./hr.	µg. P/mg (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
	2.75	1.21	22.8	422	1.95	-	-	-
		1.07	21.0	389	1.72	1.34	16.5	241
	2.65	1.14	24.6	440		1.29	21.2	310
		1.18	25.5	456	2.16	1.28	21.5	434
	2.42	1.50	14.3	321		1.23	15.6	315
		-	-	-	1.75	1.39	13.1	223
	2.20	0.84	26.9	433		1.64	18.2	310
		0.96	30.3	488	2.10	1.49	9.2	230
	2.75	1.24	18.5	358		1.40	10.3	258
		1.24	21.8	422	1.90	1.63	15.6	264
	3.07	1.07	19.9	377		1.61	15.2	257
		1.27	19.6	371	2.00	1.28	22.3	370
						1.20	21.2	352
					2.05	1.32	17.2	310
						1.39	13.6	245
N	6	11	11	11	N 8	14	14	14
Mean	2.64	1.16	22.3	407	Mean 1.95	1.39	16.5	294
S.D.	0.27	0.17	1.3	46	S.D. 0.15	0.14	4.0	58
	3.00	1.09	40.4	871	2.30	1.07	42.5	667
		1.10	44.8	966		1.07	37.7	592
	3.13	1.32	29.3	461	2.30	1.49	43.0	816
		1.35	27.1	427		1.54	40.8	774
	2.98	1.41	24.6	575	2.52	1.69	18.9	385
		1.55	23.9	558		1.71	20.8	424
	3.20	1.32	37.8	643	2.35	1.26	38.2	637
		1.42	42.5	723		1.17	30.8	513
	2.95	-	-	-	2.30	1.48	23.7	476
	3.55	1.14	33.3	666		1.48	22.5	452
		1.17	33.3	666	2.40	1.31	38.4	616
						1.40	36.1	579
					2.45	1.29	34.6	561
						1.40	33.7	546
					2.45	1.40	28.2	564
						1.01	30.4	608
N	6	10	10	10	N 8	16	16	16
Mean	3.14	1.29	33.7	656	Mean 2.38	1.36	32.5	576
S.D.	0.21	0.15	7.1	159	S.D. 0.08	0.20	7.6	112

Table VII

RAT DORSOLATERAL PROSTATE

Effect of Hypophysectomy and the Administration of ACTH on

QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact				Hypophysectomized (4 - 20 days)							
Non-treated				Non-treated				ACTH-treated			
QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity
0.85	2.43	10.8	195	0.68	1.62	16.3	222	1.10	1.06	32.1	577
	2.43	10.6	191		1.18	20.4	278		1.14	33.3	599
1.25	1.89	15.6	373	0.75	1.39	19.4	337	0.84	1.54	21.6	339
	1.92	16.0	383		1.39	20.1	350		1.57	24.5	384
1.06	-	-	-	0.70	2.29	10.1	203	0.94	2.16	14.7	202
	1.65	11.8	243		2.32	10.1	203		2.16	15.1	208
1.05	2.00	13.3	233	0.72	2.26	9.8	149	0.70	1.74	19.2	312
	2.03	12.5	219		2.33	12.1	184		1.79	19.0	309
0.87	1.64	11.6	227	0.71	1.55	24.4	322	0.75	1.51	-	-
	1.53	13.4	263		1.50	24.1	318		1.43	-	-
0.82	2.15	12.0	170	0.82	1.52	15.9	340	0.67	1.84	23.9	313
	2.15	10.7	151		1.31	17.3	271		1.74	23.4	307
0.92	1.74	8.8	162	0.82	1.56	31.4	408	0.74	1.42	23.2	338
	1.72	9.5	175		1.54	33.4	433		1.44	25.2	367
0.91	1.68	9.8	215	0.60	2.21	18.3	232	0.40	1.53	29.1	389
	1.72	10.7	235		2.39	15.3	194		1.53	32.4	433
0.90	-	-	-	0.70	1.44	25.8	346	0.57	1.56	19.4	225
0.98	1.72	18.1	323		1.42	22.9	307		1.44	22.3	258
	1.78	17.6	314	0.65	1.76	21.1	263	0.76	1.32	34.7	439
1.03	1.64	17.8	363		1.97	17.9	223		1.13	35.5	449
	1.70	19.1	389	0.65	1.76	20.7	257	0.87	0.82	43.3	515
					1.73	20.7	257		0.84	42.8	509
				0.66	0.67	46.2	624	0.79	0.99	32.9	437
					0.73	43.7	591		1.02	32.5	432
				0.92	1.18	36.9	450				
					1.20	38.5	470				
N 11	19	19	19	N 13	26	26	26	N 12	24	22	22
Mean 0.97	1.87	13.1	254	Mean 0.72	1.62	22.8	317	Mean 0.76	1.45	27.3	379
S.D. 0.12	0.26	3.2	77	S.D. 0.08	0.46	9.8	118	S.D. 0.17	0.36	7.9	109

Table VIII

RAT DORSOLATERAL PROSTATE

Effect of Hypophysectomy and the Administration of ACTH on

QO_2, Phosphorus Concentration and P^{32} Incorporation

	Intact						Hypophysectomized (4 days)					
	Non-treated			ACTH-treated			Non-treated			ACTH-treated		
	QO_2 ml O_2/gm./hr.	µg. P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm./hr	µg P/mg. (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1.11	2 56	17.1	317	1.08	1 91	19 9	429	0 80	-	-	-
		2 26	19 0	352		1.94	21.8	470	0 86	1 80	32 9	481
	0.93	1.75	15.6	279	0.95	2.00	16. 9	266		1 72	42 2	617
		1 92	15 0	268		2 00	15 9	250	1 11	1 71	22 6	457
	0 80	1.77	12.0	269	0.75	2 32	13 0	304		1 71	16 4	331
		1 80	12.2	274		2.47	14 1	329	0 80	2 04	18 9	321
	0.95	2 21	16 5	266	1 00	1 81	14 4	245		2 00	18 1	308
		1.93	16 1	259		2 11	15 6	265	0 75	1 98	12 9	323
	0.86	2.29	14 5	280	0.95	-	-	-		2 08	11 7	293
		2 40	13 7	265	1.00	2 04	13 2	264	1 10	1 82	12 9	218
	0.93	1 84	14 5	275		2 49	13.4	268		1 85	12 9	218
		1 86	15.5	294					0 88	1 58	18 3	303
										1 58	19 5	323
									1. 10	1 75	12 3	222
										1 68	12 0	217
N	6	12	12	12	6	10	10	10	8	14	14	14
Mean	0.93	2.05	15.1	283	0 96	2 11	15 8	309	0 93	1 81	18 8	331
S D.	0.10	0.27	1 9	26	0.11	0.22	2.8	75	0 14	0 16	8 5	111

	Hypophysectomized (4 days)			
	ACTH-treated			
	QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	0 78	1 85	24 4	381
		1 70	33 5	526
	0 86	1 94	21 5	408
		1 99	19 6	372
	0 99	1 43	25 0	509
		1 70	21 3	434
	0 80	2 06	9 2	193
		1 96	9 2	153
	1 23	1 88	12 8	257
		1 88	13 3	267
	0 93	1 76	16 4	263
		1 79	17 0	273
	0 85	1 61	19 3	313
		1 57	20 0	324
	0 95	1 72	12 8	256
		1 78	13 0	260
N	8	16	16	16
Mean	0 92	1 79	18 0	322
S D	0 13	0 16	6 2	106

Table IX

P R O S T A T E

Effect of the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact Guinea Pigs

Non-treated				ACTH-treated			
QO_2 ml. O_2/gm./hr	µg. P/mg (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm./hr	µg. P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
0.40				0.40	1.03		
0.25				0.48	1.32		
0.56				0.48	1.35		
0.49		-		0.37	1.18		
0.50		-	-	0.40	0.79		
0.13	-			0.47	0.81	-	
0.13	-	-	-	0.45	1.08	-	-
0.61	0.68			0.38	1.04		
0.37	0.87		-	0.10	0.74		
0.46	0.84			0.28	0.80	-	-
0.42	0.74	-	-	0.52	0.82		-
0.15	0.82	25.7	200	0.44	0.84	-	
0.45	0.83	24.5	191	0.32	1.07	25.5	820
0.26	0.85	28.1	219	0.42	1.01	-	-
0.55	0.81	27.6	215	0.44	0.96	24.4	785
0.32	4.69*	15.*	3890*	0.35	0.91	23.7	762
0.27	-	-		0.52	0.96	17.0	971
0.27	1.98*	33.3*	857*	0.32	1.03	17.1	977
0.42	-	-	-	0.40	0.83	11.8	674
0.27	0.87	27.6	512	0.33	-	-	-
0.40	0.86	35.5	659	0.39	1.05	24.0	803
0.35	0.75	30.4	564	0.43	1.02	19.6	656
0.42	0.77	31.1	577	0.49	1.01	17.4	582
0.40	2.17*	13.1*	375*	0.55	1.69	19.6	656
0.23	2.52*	9.6*	270*	0.55	0.59	23.9	741
0.43	0.97	13.1	369	0.43	0.79	14.3	562
0.23	0.89	14.4	406	0.55	0.81	17.3	537
0.53	1.09	23.3	465	-	0.69	22.6	699
0.48	1.04	24.9	497	0.43	0.92	21.0	569
0.56	1.02	24.4	487	0.48	1.07	16.2	411
0.26	1.07	22.9	457	0.39	1.32	19.0	501
0.26	1.05	22.3	608	0.57	1.28	21.5	573
0.30	1.26	16.9	461	0.30	1.41	24.1	863
0.45	1.32	17.1	466	0.42	1.72	22.5	690
0.56	1.07	16.4	447	0.60	0.99	25.2	771
				0.43	1.04	24.3	745
N 35	22	18	18	N 35	35	22	22
Mean 0.37	0.93	23.7	433	Mean 0.43	1.03	20.9	699
S.D. 0.13	0.16	6.0	139	S.D. 0.10	0.21	3.8	139

* Omitted from statistical analysis

Intact Rats

Non-treated				ACTH-treated			
QO_2 ml. O_2/gm./hr	µg. P/m. (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm./hr	µg. P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
0.86	-	-	-	1.08	-	-	-
0.99	-	-	-	1.20	0.81	23.9	
1.00	-	-	-		0.79	26.9	-
0.87	-	-	-	1.10	0.80	24.1	302
1.20	-	-	-		0.90	22.6	284
1.26	-	-	-	1.85	0.85	25.8	273
1.26	-	-	-		0.81	26.9	285
1.15	-	-	-	1.23	1.41	18.0	224
1.15	1.03	17.6	310		1.38	18.5	230
1.30	1.60	17.6	296	1.16	1.10	19.2	371
1.16	0.79	23.7	252		0.94	24.1	465
	0.62	24.1	256	1.07	0.87	16.7	261
1.40	0.92	22.6	271		0.76	19.1	298
	1.00	21.1	253	1.27	0.82	19.3	324
1.23	1.05	19.8	287		0.81	20.9	351
	0.96	22.9	331				
1.19	1.00	16.0	330				
	0.99	17.6	363				
1.16	1.20	22.8	436				
	1.44	13.6	260				
N 15	12	12	12	N 8	14	14	12
Mean 1.15	1.05	20.0	304	Mean 1.25	0.93	21.9	306
S.D. 0.15	0.25	3.3	53	S.D. 0.15	0.21	3.3	64

Table X

RAT VENTRAL PROSTATE

Effect of Hypophysectomy and the Administration of ACTH on

QO_2, Phosphorus Concentration and P^{32} Incorporation

	Intact	Hypophysectomized (4 - 20 days)		
	Non-treated	Non-treated		ACTH-treated
	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1.00	1.22	15.9	287
		1 13	18.1	327
	0 95	0.95	13.2	316
		0.93	12.4	296
	1 25	0 81	13.6	280
		0.78	12.6	259
	1 20	1.14	13 8	241
		1 00	15.3	267
	1 36	0.90	16.2	318
		0 88	15.8	310
	1 21	0 67	20.1	284
		0 68	16.3	231
	1 20	0 87	10 5	193
		0 85	7 2	132
	1 26	0 89	11.7	257
		0.90	11.6	254
	1.02	-	-	-
	1 20	0.53	28 6	510
		0 54	28.0	499
	-	0 63	27.2	554
		0.53	28.1	572
N	10	20	20	20
Mean	1 17	0 84	16.8	319
S D.	0 12	0 20	6.2	116

	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 25	0. 76	36 0	491
		0.63	43 1	588
	0 97	0 80	16 3	283
		0 82	17 4	303
	0 98	-	-	-
		1 42	13 2	265
	1 04	1 23	17 1	260
		1 33	18 4	280
	0 80	1 39	20 7	273
		1 39	21 2	280
	0 83	0 97	21 7	340
		1 02	21 4	335
	0 90	1 25	34 7	449
		1 22	36 1	468
	0 64	1 33	32 6	413
		1 27	34 0	430
	1 00	0 72	64 5	866
		0 74	64 1	860
	0 93	1 17	25 2	314
		1 17	28 5	355
	0.80	1 52	25 7	319
		1 35	28 4	352
	0. 74	1 13	33 1	447
		1 04	34 9	472
	0 95	0 76	75 8	924
		-	-	-
N	13	24	24	24
Mean	0 91	1 10	31 8	432
S D	0 15	0 26	15 8	190

	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 22	0 50	36 7	660
		0 44	40 4	727
	1 00	1 18	20 5	321
		0 93	23 9	375
	1 09	1 62	13 4	185
		1 62	14 2	196
	0 88	1 53	19 4	319
		1 59	21 0	341
	1 03	1 23	89 2	770
		1 10	65 0	561
	0 98	0 97	35 2	461
		0 95	34 9	457
	0 74	1 06	29 5	429
		1 05	29 9	435
	1 00	1 31	30 7	410
		1 26	30 0	401
	0 64	1. 36	23 3	270
		1 43	23 8	276
	0 84	1 20	23 4	296
		1 14	22 4	283
	1 25	0 75	53 0	630
		0 93	41 9	498
	1 03	0 96	37 3	495
N	12	23	23	23
Mean	0 98	1 14	33 0	426
S D	0 17	0 31	16 8	157

Table XI

RAT VENTRAL PROSTATE

Effect of Hypophysectomy and the Administration of ACTH on QO_2, Phosphorus Concentration and P^{32} Incorporation

	Intact				Hypophysectomized (4 days)			
	Non-treated		ACTH-treated		Non-treated		ACTH-treated	
	QO_2 ml. O_2/gm. /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 05	0. 65	27 3	506	0 88	0. 75	17 9	386
		0 60	22 8	422		0. 72	19 7	425
	1 15	0 64	18 6	333	1. 02	0 93	14 2	224
		0 59	20 8	372		0. 98	14 6	230
	1 15	0 80	20 1	451	0 96	0 82	11 9	278
		0. 86	17 9	401		0. 86	12 4	290
	1 00	0. 58	26 5	428	0 90	0. 86	20 1	342
		0 55	23 9	385		0 85	20 6	350
	0 96	0 59	15 4	298	1 03	-	-	-
		0. 76	15 8	306	1 10	0. 63	18 4	368
	0 92	0 61	27 7	525		0 48	19 7	394
		0. 63	27 5	521				
N	6	12	12	12	6	10	10	10
Mean	1. 04	0. 66	22 0	412	0 98	0. 79	17 0	329
S. D.	0 09	0. 09	4 4	75	0 08	0. 14	3 2	66

	Non-treated				ACTH-treated			
	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 03	-	-	-	0 96	0 92	27 5	432
	0 90	0 82	26 5	387		0 92	28 7	451
		0. 75	32 3	472	1 18	1 20	25 2	478
	1 08	0 76	17 9	362		1 22	21 2	402
		0 77	19 7	398	0 94	0 72	17 1	348
	0 90	0 82	26 7	454		0 80	16 2	330
		0 84	26 9	454	0 88	0 67	11 9	198
	1 00	1 18	11 6	290		0 69	14 0	233
		1 27	10 9	273	1 14	0 90	12 7	255
	1 06	0 84	22 2	376		0 87	12 7	255
		0 88	19 6	332	0 65	1 21	13 2	212
	0 70	0 66	22 6	375		1 14	15 0	241
		0 84	20. 1	333	1 00	0 69	26 7	433
	1 00	1 06	13 9	251		0. 71	22 7	368
		1 00	14 4	260	1 00	1 23	12 1	242
						1 06	14 7	294
N	8	14	14	14	8	16	16	16
Mean	0 96	0 89	20 4	359	0 97	0 93	18 2	323
S. D.	0 12	0. 17	6. 1	70	0 15	0. 21	5. 9	91

Table XII

R A T P L A S M A

Effect of the Administration of DCA (Acute) on Phosphorus Concentration and P^{32} Incorporation

Intact

Non-treated

Animal Weight (gm.)	P µg /ml	Specific Activity	Corrected Specific Activity
211	79	31 9	65 6
	82	30 3	
224	100	40 3	71 7
	139	23 7	
225	87	21 5	46 4
	93	19 7	
215	78	23 5	53 3
	74	26 0	
241	78	27 5	65 1
	78	24 5	
169	84	33 7	53 1
	98	29 0	
125	70	44 0	54 4
	72	42 6	
267	77	21 1	55 5
	84	20 5	
379	82	24 0	60 3
	86	19 2	
253	96	22 9	57 9
283	89	22 3	64 5
	89	23 2	
281	102	17 6	51 1
	101	18 7	
247	89	26 8	61 0
	91	22 6	
N 13	25	25	13
Mean 232	88	25 4	58 5
S D	14	7 3	6 8

DCA (Acute)

Animal Weight (gm.)	P µg /ml	Specific Activity	Corrected Specific Activity
222	74	29 3	65 9
	78	30 1	
233	80	21.7	54 5
	84	25 0	
259	69	25 1	71 5
	69	30 0	
161	82	33 4	52 6
	91	32 0	
129	63	45 4	58 8
	61	45 8	
264	110	20 8	63 1
	74	26 9	
263	72	21 9	56 5
	74	21 0	
284	115	18 6	51 1
	113	17 4	
265	79	25 3	61 7
	89	21 2	
270	89	22 1	59 9
	91	22 2	
249	89	16 4	42 3
	89	17 6	
N 11	22	22	11
Mean 236	83	25 9	58 0
S D	15	7 8	7 6

Table XIII

R A T P L A S M A

Effect of Adrenalectomy and the Administration of DCA (Chronic) on Phosphorus Concentration and P^{32} Incorporation

Intact

Non-treated

Animal Weight (gm.)	P mg /ml.	Specific Activity	Corrected Specific Activity
168	73	35 5	63 8
	72	40 4	
135	71	41 2	57 0
	65	43. 1	
143	82	37 6	53. 3
	88	37 0	
161	98	30 7	48 6
	70	29 7	
158	89	29 4	48 2
	91	31 5	
150	98	58 8	84 8
	104	54 2	
193	66	26 3	53 1
	68	28 7	
203	66	20 2	37 8
	68	17 0	
201	68	24 4	47 8
	69	23 2	
177	70	27 0	46 9
	68	25 9	
N 10	20	20	10
Mean 169	77	33 1	54 1
S D	12	10 3	12 1

DCA (Chronic)

Animal Weight (gm)	P µg /ml	Specific Activity	Corrected Specific Activity
186	69	30 4	52 6
	81	26 1	
174	85	31 7	53 4
	87	29 7	
175	83	32 6	58 8
	74	34 5	
190	99	16 6	28 9
	108	13 7	
198	104	27 6	56 6
	101	29 6	
192	92	35 4	70 7
	81	38 2	
197	90	11 4	22 9
	92	11 7	
162	87	41 9	72 3
	85	47 2	
214	94	28 8	58 9
	94	26 1	
221	81	4 7	10 4
	85	4 7	
N 10	20	20	10
Mean 191	89	26 1	48 6
S D	10	11 6	19 7

Adrenalectomized

Non-treated

Animal Weight (gm)	P µg /ml	Specific Activity	Corrected Specific Activity
192	83	35 4	68 7
	81	36 2	
176	77	42 9	75 3
	73	42 7	
186	55	39 7	71 6
	95	37 2	
154	77	45 5	63 8
	90	47 1	
198	81	31 9	62 2
	81	31 9	
180	79	35 6	63 5
	90	35 0	
191	133	39 4	77 0
	122	41 1	
164	121	65 0	105 8
	118	64 0	
192	85	87 6	159 0
	94	78 0	
181	-	-	-
167	-	-	-
155	-	-	-
N 12	18	18	9
Mean 178	91	45 9	83 0
S D	20	15 9	29 6

DCA (Chronic)

Animal Weight (gm)	P µg /ml	Specific Activity	Corrected Specific Activity
190	99	27 7	58 1
	103	33 5	
166	70	49 4	83 5
	70	51 1	
205	70	36 4	76 5
	70	38 1	
187	90	37 0	73 9
	81	42 0	
192	84	35 6	65 7
	95	32 8	
166	86	40 8	67 2
	90	40 1	
179	121	10 4	22 2
	112	14 4	
208	101	25 1	56 2
	92	29 2	
165	-	-	-
188	92	38 0	73 3
	90	39 9	
205	83	33 6	70 7
	83	35 3	
218	92	28 0	61 9
	92	28 7	
224	94	26 1	60 7
	83	28 0	
191	-	-	
N 14	24	24	12
Mean 192	89	33 4	64 2
S D	13	9 1	14 8

Table XIV

R A T A D R E N A L

Effect of the Administration of DCA on QO_2, Phosphorus Concentration and P^{32} Incorporation

DCA (Acute)

Non-treated

QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
2 07	1.27	27 4	418
	1 52	28 2	430
2 35	1 61	24 1	336
	1 39	28 0	391
2 63	1 61	14 2	306
	1 62	14 5	313
2 67	1.12	25 4	477
	1 17	22 8	428
2 75	1 08	28 6	439
	1 14	29 5	453
2 60	1 79	17 5	330
	1 85	17 0	320
3 20	1 83	52 2	960
	1.77	52 4	963
3 20	0 65	34 2	616
	0 78	29 2	526
2 40	0 85	25 0	344
	0 85	23 9	387
2 27	0 99	19 9	405
	1 04	22 4	406
2 10	0 91	26 1	546
	1 00	26 2	490
-	0 93	33 3	415
	0 93	29 9	396
N 11	24	24	24
Mean 2 57	1 24	27 2	462
S D 0 37	0 37	9 2	168

DCA-treated

QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
2 95	2.03	21.2	322
	1 84	22 9	348
3 28	0 73	28 1	516
	0 94	27 1	497
3 20	1.51	21 2	297
	1 45	23 0	322
3 05	1.10	25 5	485
	1 45	23 6	449
2 52	1.26	42 6	724
	1 84	36 4	619
2 92	0 85	22 2	352
	0 85	22 2	352
3 27	0 88	25 3	448
	0 80	28 4	503
2 60	1.03	19 2	376
	1 03	17 0	333
2 86	0 96	22 5	365
	0 96	21 1	342
-	0 98	28 6	477
	0 91	27 6	461
N 9	20	20	20
Mean 2.96	1 17	25 3	429
S D 0 26	0.37	5 7	107

DCA (Chronic)

Non-treated

QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
2 45	1 18	15 7	246
	1 33	15 8	248
2 55	1 00	45 3	795
	1 28	10 0	702
3 23	1 33	38 9	730
	1 27	38 3	719
2 80	1 70	27 5	566
	1 70	27 3	562
2 95	1 06	23 5	488
	1 08	24 5	508
2 70	0 98	30 3	357
	1 03	28 8	340
2 43	0 79	30 0	565
	0 82	30 4	573
2 37	0 95	12 8	339
	0 98	13 0	344
2 10	0 99	12 5	262
	1 02	14 0	293
-	1 04	18 2	388
	1 04	17 3	369
N 9	20	20	20
Mean 2 62	1 13	25 2	470
S D 0 32	0 24	9 9	171

DCA-treated

QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
2 20	0 98	31 0	585
	0 98	32 3	609
2 30	1 59	19 4	442
	1 69	20 1	458
2 35	-	-	-
2 27	1 12	11 6	248
	1 08	13 7	293
2 60	1 18	27 8	385
	1 02	31 8	440
2 57	0 95	4 9	141
	0 82	6 1	176
N 6	10	10	10
Mean 2 38	1 14	19 9	378
S D 0 15	0 27	10 0	152

Table XV

RAT DORSOLATERAL PROSTATE

Effect of the Administration of DCA (Acute) on QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact

Non-treated

QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
0 80	2 08	16 0	244
	1 89	17 4	265
1.03	2. 19	18 6	259
	2 53	15 7	219
0 99	2 02	11 8	254
	2 02	11 9	256
1 00	1 76	12 7	238
	1 67	11 3	212
0. 75	1. 79	14 8	227
	1 83	13 8	212
0 90	1 95	18 4	347
	2 24	16 5	311
1 20	1 84	20 9	384
	1. 78	21 6	397
0. 91	1. 69	14 6	263
	1 69	15 6	281
0 85	2 17	12 4	206
	2 29	13 0	216
0 84	2 37	11 3	195
	2 11	11 3	195
0 75	1 79	11 3	175
	1 77	12 2	189
-	1 63	17 5	343
	1. 71	16 4	321
-	2 44	11 5	189
	2 55	11 1	182
N 11	26	26	26
Mean 0 91	1 99	14 6	253
S D 0 13	0. 28	3 1	62

DCA (Acute)

QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
0 90	2 10	13 0	197
	1 93	14 9	226
0 93	1 92	10 1	185
	1 62	13 3	244
0 68	1 05	25 3	354
	1 07	24 7	345
1 00	1 81	21 0	399
	2 06	16 3	310
0 83	1 81	-	-
	1 61	18 5	315
0 62	1 98	12 6	200
	1 96	11 9	189
0 93	1 86	14 9	264
	2 00	11 9	211
0 96	1 81	13 2	258
	2 00	11 0	215
0 76	2. 09	15 9	258
	2. 04	16 1	261
-	2 00	15 3	255
	1. 92	15 8	264
-	2 08	9 1	215
	2 11	8 6	203
N 9	22	21	21
Mean 0 85	1 86	14 9	256
S D. 0 12	0. 29	4 4	58

Table XVI

RAT DORSOLATERAL PROSTATE

Effect of Adrenalectomy and the Administration of DCA (Chronic) on QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact					Adrenalectomized				
Non-treated		DCA (Chronic)			Non-treated		DCA (Chronic)		
QO_2 ml O_2/gm./hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity		QO_2 ml O_2/gm./hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity	
1.00	2.42	19.0	298		-	1.53	21.0	306	
	1.73	20.5	321			1.84	21.5	313	
0.90	1.54	27.4	181		1.03	1.39	21.3	283	
	1.68	28.3	497			1.73	21.5	286	
1.25	1.38	26.2	492		0.86	1.50	20.0	279	
	2.69	25.3	475			1.59	20.0	279	
0.85	1.86	17.0	350		0.55	1.58	11.5	180	
	1.78	17.3	356			1.43	13.2	207	
0.72	1.71	16.3	338		0.75	1.19	22.6	363	
	1.55	15.6	324			1.58	21.3	342	
0.90	1.62	18.1	213		0.73	1.25	20.5	323	
	1.56	17.5	206			1.14	24.7	389	
0.95	1.42	15.1	284		0.70	2.07	14.8	192	
	1.44	18.0	339			2.07	13.7	178	
1.00	1.41	11.4	302		0.90	2.01	19.0	180	
	1.49	11.6	307			1.92	18.3	173	
0.95	1.70	10.0	209		0.85	2.05	15.3	96	
	1.77	10.6	222			2.08	12.9	81	
-	1.84	13.8	294		0.80	-	-	-	
	1.57	16.9	360		0.56	1.61	22.6	-	
						1.61	24.7	-	
					0.75	-	-	-	
N 9	20	20	20		N 11	20	20	18	
Mean 0.95	1.71	17.8	333		Mean 0.77	1.66	19.0	247	
S.D. 0.13	0.32	5.3	90		S.D. 0.13	0.30	3.9	87	

QO_2 ml O_2/gm./hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
0.65	1.53	18.9	359
	1.58	19.3	367
0.90	1.13	24.2	453
	0.98	28.9	541
1.00	1.88	23.1	393
	1.90	22.5	383
0.75	2.09	6.7	232
	2.21	5.8	201
0.75	1.93	17.7	313
	1.95	16.2	286
0.57	-	-	-
0.75	1.54	23.7	535
	1.67	24.7	349
0.80	1.86	3.3	144
	1.88	2.4	105
0.75	1.68	30.5	422
	1.70	29.8	412
0.65	1.50	11.9	202
	1.35	10.0	170
0.82	-	-	-
N 11	18	18	18
Mean 0.76	1.69	17.8	315
S.D. 0.11	0.31	8.9	114

QO_2 ml O_2/gm./hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
0.63	2.38	14.8	255
	2.26	14.9	256
1.20	1.90	24.2	290
	1.54	23.5	281
0.62	1.58	17.7	231
	1.74	15.9	208
0.82	1.47	18.9	256
	1.43	17.4	235
0.70	-	-	-
0.39	0.75	30.2	449
	0.82	28.8	429
0.80	1.92	2.0	90
	1.70	3.2	144
0.95	1.95	17.7	313
	1.75	19.0	336
0.83	-	-	-
0.94	1.23	26.4	360
	1.13	30.4	415
0.85	1.83	19.7	279
	2.07	18.6	263
0.50	3.51	9.4	152
	3.51	8.8	142
0.54	2.02	14.0	231
	1.77	16.1	265
0.72	-	-	-
N 14	22	22	22
Mean 0.75	1.83	17.8	267
S.D. 0.20	0.67	7.5	91

Table XVII

RAT VENTRAL PROSTATE

Effect of the Administration of DCA (Acute) on QO_2, Phosphorus Concentration and P^{32} Incorporation

Intact

Non-treated

	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 20	0 84	27 7	422
		0 90	28 0	427
	1 44	0 60	29 7	414
		0 72	23 7	331
	1 05	0 92	16 1	347
		0 88	15 9	343
	1 18	0 85	21 6	405
		0 85	21 2	398
	1 40	0 85	19 6	301
		0 83	20 2	310
	1 06	1 03	25 9	488
		1 07	24 0	452
	1 30	1 21	22 0	404
		1 20	23 6	434
	1 26	0 72	24 0	398
		0 71	26 1	433
	1 26	0 71	26 6	459
		0 70	26 2	453
	1 06	0 63	23 8	466
		0 67	23 1	452
	1 23	0 64	29 3	480
		0 66	27 7	454
N	11	22	22	22
Mean	1 22	0 83	23 9	412
S D	0 13	0 17	3 7	53

DCA (Acute)

	QO_2 ml. O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 17	0 96	21 8	331
		1 01	21 0	319
	1 18	0 78	16 5	303
		0 77	19 2	352
	1 21	0 91	21 6	302
		0 98	20 1	281
	1 43	0 78	26 0	494
		0 74	25 4	483
	1 25	0 93	24 2	412
		0 96	24 5	417
	1 37	0 70	19 0	301
		0 68	23 7	376
	1 12	0 75	20 3	359
		0 65	25 0	442
	1 21	0 55	19 7	386
		0 59	21 5	421
	1 04	0 70	24 6	399
		0 70	26 6	431
	-	0 56	29 8	497
		0 61	-	-
	-	0 72	18 5	437
		0 70	20 1	475
N	9	22	21	21
Mean	1 22	0 76	22 3	391
S D	0 11	0 14	3 2	67

Table XVIII

RAT VENTRAL PROSTATE

Effect of Adrenalectomy and the Administration of DCA (Chronic) on QO_2, Phosphorus Concentration and P^{32} Incorporation

	Intact			
	Non-treated		DCA (Chronic)	
	QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 00	0 66	25 4	398
		0 66	27 8	436
	-	0 63	32 8	576
		0 69	37 1	651
	0 95	0 62	20 4	383
		0 52	30 8	578
	1 05	0 61	26 6	547
		0 78	31 2	642
	1 33	0 60	29 0	602
		0 59	33 9	703
	1 25	0 73	30 3	357
		0 66	32 0	377
	1 25	0 64	17 5	330
		0 64	16 3	307
	1 14	0 59	14 5	384
		0 60	13 9	368
	0 98	0 67	21 1	441
		0 70	19 7	412
	-	0 70	21 3	454
		0 71	21 2	452
N	8	20	20	20
Mean	1 12	0 66	25 1	470
S D	0 14	0 06	6 7	116

	Intact			
	Non-treated		DCA (Chronic)	
	QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 15	0 71	23 5	447
		0 73	24 7	470
	1 18	0 83	24 7	463
		0 68	32 4	607
	1 15	1 12	29 1	495
		1 06	28 8	490
	1 25	0 96	7 9	273
		0 97	10 6	367
	1 35	1 01	28 5	504
		1 09	27 6	488
	0 80	-	-	-
	1 25	0 92	33 0	467
		0 88	37 4	529
	0 90	1 06	4 7	205
		1 06	5 3	231
	1 32	0 57	46 2	639
		0 55	43 0	595
	1 44	0, 83	20 3	345
		0 83	21 0	357
	1 32	-	-	
N	11	18	18	18
Mean	1 19	0 88	24 9	443
S D	0 19	0 17	11 6	121

	Adrenalectomized			
	Non-treated		DCA (Chronic)	
	QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 50	0 73	32 4	472
		0 75	31 6	460
	1 15	0 98	31 6	420
		0 95	33 6	446
	1 17	0 50	31 6	441
		0, 48	30 2	422
	1 00	0 92	32 9	516
		0 98	28 7	450
	1 23	0 71	28 7	461
		0 73	30 2	486
	1 30	0 79	37 0	583
		0 73	32 4	510
	0 84	0 60	30 7	399
		0 61	24 6	319
	0 90	0 76	31 6	299
		0 84	29 8	282
	1 30	0 62	18 3	115
		0 57	22 1	139
	0 90	-	-	-
	0 87	0 78	36 0	-
		0 84	35 5	-
	1 00	-	-	-
N	12	20	20	18
Mean	1 10	0 74	30 5	401
S D	0 20	0 15	4 4	122

	Adrenalectomized			
	Non-treated		DCA (Chronic)	
	QO_2 ml O_2/gm /hr	µg P/mg (Wet Weight)	Specific Activity	Relative Specific Activity
	1 05	0 67	25 9	446
		0 65	26 7	460
	0 65	0 61	34 5	413
		0 61	32 6	390
	1 30	0 84	28 3	370
		0 82	28 1	367
	-	0 67	41 8	566
		0 74	37 2	503
	1 07	0 65	33 8	514
		0 61	37 7	574
	0 80	0 77	31 0	461
		0 75	26 0	387
	0 90	0 58	6 3	284
		0 48	12 1	545
	1 20	0 82	30 7	542
		0 82	34 0	601
	1 00	-	-	-
	1. 10	0 76	35 5	484
		0 86	34 6	472
	1 14	0 63	33 3	471
		0 68	33 1	468
	1 05	0 46	38 2	617
		0 55	30 6	494
	1 30	0 82	23 8	392
		0 77	26 5	437
	1 00	-	-	-
N	13	24	24	24
Mean	1 04	0 69	30 1	469
S D	0 18	0 11	7 7	80